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15 HEMATOLOGIC ASSESSMENT

15.1 INTRODUCTION

15.1.1 Background

Experiments in laboratory animals have demonstrated that 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) is directly toxic to the hematopoietic system in several species. In one study, dioxin administered in low doses (0.70 μg/kg or 350 μg/kg of dioxin by oral gavage) to monkeys resulted in elevated neutrophil counts while higher doses were associated with lympho- and thrombocytopenia (1). A decrease in overall cellularity and an increase in the myeloid-erythroid ratio were noted in approximately half of the sternal bone marrow samples examined at the conclusion of the experiment.

Other animal studies have shown that the toxic effects of dioxin on the hematopoietic system vary depending on the dose employed and the species examined. In many reports, it is difficult to distinguish primary effects from those occurring secondary to systemic toxicity. One study in rats using gavage doses of dioxin varying from 0.001 to 1.0 μg/kg noted depressed red blood cell (RBC) counts and packed cell volumes in the high-dose group (2). In another rat experiment employing 10 μg/kg of dioxin orally, elevated erythrocyte, reticulocyte, and neutrophil counts were noted with reduction in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet counts, and clot retraction times—effects that the authors felt could be attributed to systemic toxicity with terminal dehydration (3). In a multispecies study, mice and guinea pigs given oral doses of dioxin varying from 0.1 μg/kg to 50 μg/kg were found to have dose-dependent reductions in leukocytes with relative lymphocytopenia within 1 week of dioxin administration, and thrombocytopenia and hemoconcentration were found in rats (4).

Several animal experiments, although designed primarily to investigate immunologic sequelae of dioxin exposure, have focused on selected hematologic elements, particularly macrophages and polymorphonuclear leukocytes, but whether the responses observed were secondary to inflammation or specific to dioxin is not known (3, 5–7).

More recent animal research relevant to the hematopoietic system has focused on the altered cellular differentiation associated with dioxin toxicity. In mice, progenitor cells were suppressed following exposure to dioxin in doses as low as 1.0 μg/kg of body weight, and in vitro studies demonstrated that myelotoxicity occurs by a direct inhibition of proliferating stem cells (8). A subsequent study from the same laboratory demonstrated a direct effect of dioxin on cultured lymphocytes resulting in a selective inhibition of B-cell differentiation into antibody-secretive cells (9). In these and other studies (10), the authors cite evidence for the role of the aryl hydrocarbon (Ah) receptor in mediating these myelo- and lymphotoxic effects. In another report, the presence of the Ah receptor was defined in the spleens of numerous primate species (11). Although Ah receptors have been isolated in the tissue of several human organs (12–17), the relevance of these observations to dioxin hematopoietic toxicity remains to be proven (18).

In general, human observational studies have shown fewer and less consistent hematologic findings than the structured animal experiments. Mortality and morbidity studies that have included hematologic data as endpoints have been based on populations exposed to dioxin by occupation (19–21), environmental contamination (22–26), consequent to industrial chemical accidents (27–33), and during military service in Southeast Asia (SEA) (34–39).

In the cancer mortality study reported by the National Institute of Occupational Safety and Health, one of few to incorporate serum dioxin data into the analyses, there was no significant increase in the relative risk of hematologic malignancies associated with exposure to dioxin in either the entire cohort or in a subcohort with more than 20 years of latency (19). Numerous studies have been conducted on cohorts that were exposed to dioxin by contamination of soil at the Quail Run (22–24) and Times Beach (25) residential areas of Missouri. With one exception, no differences were found in any of the hematologic parameters examined. In the Times Beach study, a statistically significant increase in the mean platelet count was noted in the exposed cohort relative to the unexposed, but the difference (281,927 mm^3 vs. 249,061 mm^3) was not considered clinically meaningful. A follow-up study, the first to report clinical hematologic indices in relation to tissue levels of dioxin (26), found no abnormalities in the complete blood count related to the body burden of dioxin.

A clinical epidemiological study was conducted 30 years after an explosion in a trichlorophenol plant in Nitro, West Virginia. The study compared 204 highly exposed employees, 86 percent of whom had developed chloracne, with 163 employees who were not exposed (27). No significant differences were found in the standard hematologic indices. A recent mortality experience study of 754 workers employed at the same plant, 122 of whom had sufficiently severe dioxin exposure to cause chloracne, found no increased mortality associated with all lymphatic and hematopoietic malignancies (32).

The monitoring of the populations heavily exposed to dioxin during the Seveso, Italy, hexachlorophene manufacturing plant explosion in 1976 and at the BASF chemical plant in 1953 continues to generate reports of medical surveillance. Although transient depression of the peripheral white blood cell (WBC) count after dioxin exposure has been documented (20, 21), a morbidity study of workers involved in the cleanup of the Seveso environs found no differences in selected hematologic indices (hemoglobin, WBC count, and platelets) between exposed subjects and controls (33). In the most recent report on the BASF population, exposed subjects had a significantly higher erythrocyte sedimentation rate than referents (6.53 mm/hr vs. 4.95 mm/hr), but no differences were noted in the WBC count, platelet count, or hemoglobin (20).

In previous reports of the Air Force Health Study (AFHS) (35–37), Ranch Hand participants were found to have slightly higher mean platelet counts than Comparisons and, in the 1987 follow-up examinations (37), a significantly greater percentage of abnormally high platelet counts as well. In the serum dioxin analysis of the 1987 examinations (38), Ranch Hands with the highest current serum dioxin levels had higher mean platelet and total WBC counts than Comparisons, results that raised the possibility of a chronic inflammatory response associated with dioxin levels. In the 1992 examinations, when the results were adjusted for covariates, no significant group differences were noted between the Ranch Hand and Comparison cohorts, nor was there any evidence for a persistent inflammatory response related to prior exposure to dioxin (39).

15.1.2 Summary of Previous Analyses of the Air Force Health Study

15.1.2.1 1982 Baseline Study Summary Results

The functional integrity of the hematopoietic system was assessed at the 1982 baseline examination by the measurement of eight peripheral blood variables: RBC count, WBC count, hemoglobin, hematocrit, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), and platelet count. These variables were analyzed in the discrete form to detect differences in the percentages of values outside the designed laboratory range, as well as analyzed in the continuous form to detect shifts in mean values between the Ranch Hand and Comparison groups.

The Ranch Hand group had a significantly higher adjusted mean MCV and MCH than the Comparison group (p=0.05 and p=0.04, respectively), although the magnitude of the difference was small in each case. The Ranch Hand adjusted mean values for five other parameters (i.e., RBC, WBC, hemoglobin, hematocrit, and MCHC) were nearly identical to the adjusted mean values of the Comparison group. The mean platelet count for Ranch Hands was marginally significantly greater than the Comparison mean count (p=0.06). The percent of abnormal values for these eight variables, as established by the upper and lower limits of normal, did not differ significantly between the two groups.

15.1.2.2 1985 Follow-up Study Summary Results

The same eight peripheral blood variables (i.e., RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count) were analyzed in the 1985 follow-up study. The unadjusted discrete analysis of the percent abnormal values, both low and high, showed no statistically significant difference between the Ranch Hand and Comparison groups for any of the hematologic variables. Similarly, in the adjusted discrete analyses, none of the adjusted relative risks was significant.

As no subgroup demonstrated consistent patterns of hematologic impairment, biologic relevance was not assigned to the interactions. The significant group differences found for MCV and MCH at the baseline examination were not present in the 1985 follow-up analyses. The covariate effects of age, race, occupation, and lifetime smoking history were highly significant for many of the hematologic variables.

The longitudinal analyses of MCV, MCH, and platelet count found a significant group difference for platelet count, with the Ranch Hands having an average decrease in platelet count between examinations and the Comparisons having an average increase. As a result, the baseline group difference (nonsignificant) in mean values approached equality at the 1985 follow-up examination.

In conclusion, none of the eight hematologic variable means was found to differ significantly between the Ranch Hand and Comparison groups. The expected effects of age, race, and smoking were demonstrated with most of the hematologic variables. The longitudinal analyses also suggested that neither group manifested an impairment of the hematopoietic system. Exposure index analyses did not support a plausible dose-response relation for any of the hematologic variables.

15.1.2.3 1987 Follow-up Study Summary Results

The hematologic status of the Ranch Hand and Comparison groups was assessed by the examination of the same eight variables used in the two previous examinations: RBC, WBC, hemoglobin, hematocrit, MCV, MCH, MCHC, and platelet count. There were no statistically significant differences between the Ranch Hand and Comparison groups for mean RBC count, hemoglobin, hematocrit, MCV, MCH, and MCHC, in analyses either unadjusted or adjusted for the covariates of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history. For WBC count, the unadjusted mean level was significantly greater in Ranch Hands than in Comparisons. The difference was not statistically significant after adjustment for covariates, nor were significant differences detected in the percentage of individuals with abnormal values.

Mean platelet counts also were significantly greater in Ranch Hands than in Comparisons, as was the percentage of individuals with abnormally high platelet counts. Longitudinal analyses detected a significantly greater decrease in the mean platelet count in Ranch Hands than in Comparisons, despite the higher overall mean count, from the baseline examination to the 1987 follow-up examination.

15.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

The number of dependent hematologic variables was increased from eight to nine with the addition of prothrombin time. Several of the nine variables showed an association with initial dioxin in the unadjusted model, but when the model was adjusted for covariates, the associations became nonsignificant. Hemoglobin and hematocrit were positively associated with current dioxin when time since duty in SEA was no more than 18.6 years and negatively associated with current dioxin when time since duty in SEA was greater than 18.6 years. For the discrete RBC count analysis, the relative risk of an abnormally low count was less than one when time since duty in SEA did not exceed 18.6 years and was greater than one when time since duty in SEA was more than 18.6 years. Because a low RBC count was considered abnormal for the purpose of these statistical analyses, the trend in relation to current dioxin was similar to that in the continuous analyses of hemoglobin and hematocrit. In the discrete analysis of prothrombin time, the trend in relation to current dioxin also was similar to that in the continuous analyses of hemoglobin and hematocrit. In the categorized current dioxin analyses, whenever the overall contrast showed significant, or marginally significant, differences among the categories, the mean level or percent abnormal in the three categories of Ranch Hands (i.e., officers, enlisted flyers, and enlisted groundcrew) tended to exceed the corresponding mean level or percent abnormal in the background category that consisted of Comparisons. The longitudinal analyses of MCV, MCH, and platelet count displayed no significant associations with dioxin.

In summary, the results of the previous analysis revealed no meaningful association between hematopoietic toxicity and dioxin exposure. Statistical analyses of two variables (WBC and platelet count) raised the possibility of subtle biologic effects that cannot be considered clinically meaningful but did point to the need for follow-up in future AFHS examinations. The increased platelet and WBC counts, in addition to the elevation of erythrocyte sedimentation rates (in the general health assessment), were thought to indicate the presence of a chronic inflammatory response to dioxin exposure.

15.1.2.5 1992 Follow-up Study Summary Results

The number of dependent hematologic variables was increased from 9 to 13 with elimination of MCV, MCH, and MCHC and the addition of RBC morphology (normal, abnormal), absolute neutrophils (segs), absolute neutrophils (bands), absolute lymphocytes, absolute monocytes, absolute eosinophils, and absolute basophils. The 13 endpoints analyzed in the hematology assessment provided a comprehensive evaluation of the three peripheral blood lines (erythrocytes, leukocytes, and platelets) and their relation to dioxin exposure. In the analyses of these variables, only platelet count exhibited significant associations with the herbicide exposure indices. Ranch Hands in the enlisted flyer and enlisted groundcrew categories possessed statistically significant higher mean platelet counts than Comparisons, although the result was not considered meaningful from a clinical point of view. Analyses using extrapolated levels of initial dioxin showed that Ranch Hands with high dioxin levels had significantly greater mean platelet count measurements than Comparisons. Platelet counts also were positively associated with current serum dioxin measurements, although the association became nonsignificant when adjusted for covariates. The 1992 follow-up results supported the results found in both the 1987 follow-up study and in the serum dioxin analysis of the 1987 follow-up study, but the biologic meaning was uncertain. Results from the 1987 follow-up study generated questions regarding the possibility of a subclinical inflammatory response associated with prior dioxin exposure. This was due to elevated mean WBC counts, platelet counts, and erythrocyte sedimentation rates in Ranch Hands. The 1992 follow-up study did not produce significant results to support this possibility. Therefore, in conclusion, there was no evidence from the 1992 follow-up study that suggested an association between hematopoietic toxicity and prior dioxin exposure.

15.1.3 Parameters for the 1997 Hematologic Assessment

15.1.3.1 Dependent Variables

The analysis of the hematologic assessment consisted of data from the laboratory examination only. No questionnaire or physical examination data were analyzed.

15.1.3.1.1 Laboratory Examination Data

A total of 13 hematology variables measured at the laboratory as part of the 1997 follow-up examination were analyzed statistically. These variables were the same as those studied in 1992 and included five cell counts, one RBC morphology, six measures of absolute blood counts, and a coagulation measure (prothrombin time). These variables were determined by routine hematologic procedures. In particular, the cell count indices were performed on the Coulter STKS® automated instrument, and prothrombin time was measured on the AMAX CS-190® instrument. All dependent variables were analyzed in the continuous form, except for the RBC morphology. RBC count, WBC count, hemoglobin, hematocrit, platelet count, prothrombin time, and the RBC morphology also were analyzed in their discrete form, using Scripps Clinic normal ranges as cutpoints. RBC count, WBC count, hemoglobin, hematocrit, and platelet count were trichotomized as abnormal low, normal, and abnormal high.

RBC morphology was constructed from a number of laboratory conditions, many of which were minor abnormalities. Conditions considered to be abnormal for the 1997 follow-up included rouleaux, Burr cells, moderate microcytes, many microcytes, moderate macrocytes, moderate amount of ovalocytes, hypochromia, anisocytosis, slight polychromasia, slight baso-stippling, moderate stomatocytes, schistocytes, Howell-Jolly bodies, few teardrop cells, and Papperheimer bodies. Participants with few ovalocytes, few microcytes, few macrocytes, and slight macrocytes were considered to be normal for RBC morphology.

Participants testing positive for the human immunodeficiency virus (HIV) were excluded from the analysis of all variables. Participants with a fever (body temperature greater than or equal to 100° Fahrenheit) at the time of the examination were excluded from the analysis of all variables except prothrombin time. Participants taking an anticoagulant (such as Coumadin®) or aspirin at the time of the examination also were excluded from the analysis of prothrombin time. In addition, one participant had a hemolyzed specimen for prothrombin time and was excluded from the analysis of this variable.

15.1.3.2 Covariates

Age, race, military occupation, current level of cigarette smoking (cigarettes/day), and lifetime cigarette smoking history (pack-years) were used as covariates in adjusted statistical analyses evaluating the hematologic dependent variables.

Age, race, and military occupation were determined from military records. Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

15.1.4 Statistical Methods

Table 15-1 summarizes the statistical analyses performed for the hematologic assessment. The first part of this table describes the dependent variables analyzed. The second part of this table provides a further description of the covariates examined. A covariate was used in its continuous form whenever possible for all adjusted analyses; if necessary, if the covariate is inherently discrete (e.g., military occupations), or if a categorized form was needed to develop measures of association with the dependent variables, the

covariate was categorized as shown in Table 15-1. Table 15-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 15-1. Statistical Analysis for the Hematologic Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
RBC Count (million/mm^3)	LAB	D/C	Abnormal Low: <4.3 Normal: 4.3–5.9 Abnormal High: >5.9	(1)	(a)	U:PR,GLM A:PR,GLM
WBC Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <4.5 Normal: 4.5–11.0 Abnormal High: >11.0	(1)	(a)	U:PR,GLM A:PR,GLM
Hemoglobin (gm/dl)	LAB	D/C	Abnormal Low: <13.9 Normal: 13.9–18.0 Abnormal High: >18.0	(1)	(a)	U:PR,GLM,CS A:PR,GLM
Hematocrit (percent)	LAB	D/C	Abnormal Low: <39.0 Normal: 39.0–55.0 Abnormal High: >55.0	(1)	(a)	U:PR,GLM,CS A:PR,GLM
Platelet Count (thousand/mm^3)	LAB	D/C	Abnormal Low: <130 Normal: 130–400 Abnormal High: >400	(1)	(a)	U:PR,GLM,CS A:PR,GLM L:PR,GLM
Prothrombin Time (seconds)	LAB	D/C	High: >12.3 Normal: ≤12.3	(1)	(b)	U:LR,GLM,CS A:LR,GLM
RBC Morphology	LAB	D	Abnormal Normal	(1)	(a)	U:LR A:LR
Absolute Neutrophils (segs) (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Neutrophils (bands) (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM
Absolute Lymphocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Monocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
Absolute Eosinophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM
Absolute Basophils (thousand/mm^3)	LAB	D/C	Zero Nonzero	(1)	(a)	U:LR,GLM A:LR,GLM

[a]Covariates:
(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history.

Table 15-1. Statistical Analysis for the Hematologic Assessment (Continued)

[b]Exclusions:
(a): participants with body temperatures greater than or equal to 100° Fahrenheit, participants testing positive for HIV.
(b): participants testing positive for HIV, participants taking an anticoagulant (such as Coumadin®) or aspirin at the time of the examination.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
Q-SR: Health questionnaires (self-reported)

Data Form: C: Continuous analysis only
D: Discrete analysis only
D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 15-2. Number of Participants Excluded or with Missing Data for the Hematology Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Platelet Count	DEP	4	6	2	4	4	6
Prothrombin Time	DEP	0	1	0	0	0	1
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Body Temperature ≥100° Fahrenheit at the Time of the Physical Exam	EXC	1	0	1	1	1	0
HIV Positive	EXC	3	2	3	3	3	2
Taking an Anticoagulant or Aspirin at the Time of the Physical Exam	EXC	179	232	104	176	176	223

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

Absolute neutrophils (bands), absolute eosinophils, and absolute basophils had a large number of measurements equal to 0 counts per mm^3. The nonzero measurements exhibited a positively skewed distribution, and a logarithmic transformation, however, was applied to achieve an approximate normal distribution. The logarithmic transformation, however, could not be applied to the measurements equal to 0 counts per mm^3. Consequently, these variables were analyzed in two forms: (a) a continuous analysis of the nonzero measurements and (b) a discrete analysis of the proportion of zero measurements.

15.1.4.1 Longitudinal Analysis

Longitudinal analyses on platelet count were conducted to evaluate the association of exposure to mean changes between the 1982 baseline examination and the 1997 follow-up examination.

15.2 RESULTS

15.2.1 Dependent Variable-Covariate Associations

Tests of associations were performed for each dependent variable in the hematology assessment with each covariate. Results are displayed in Appendix F, Table F-7. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants who tested positive for HIV or who had a body temperature greater than or equal to 100° Fahrenheit were excluded from the analysis of all variables except prothrombin time. The analysis of prothrombin time included all participants except those testing positive for HIV or those taking an anticoagulant or aspirin at the time of the examination. In addition, one participant had a hemolyzed specimen for prothrombin time and was excluded from the analysis of this variable.

RBC count in its continuous form displayed a significant association with age ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p=0.003$), and lifetime cigarette smoking history ($p=0.031$). RBC count decreased as age increased ($r=-0.181$). Among the occupational strata, enlisted groundcrew displayed the highest mean RBC count (5.01 million/mm^3), followed by enlisted flyers (4.95 million/mm^3), then officers (4.90 million/mm^3). RBC count increased as current cigarette smoking increased ($r=0.064$). Conversely, as lifetime cigarette smoking increased, RBC count decreased ($r=-0.047$).

Tests of covariate associations involving RBC count in its discrete form revealed significant findings for age ($p=0.001$) and race ($p=0.001$). The prevalence of both low and high RBC abnormalities were higher among older participants and among Blacks.

Significant associations were found between WBC count in its continuous form and race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Non-Blacks had a higher mean WBC count (6.71 thousand/mm^3) than did Blacks (5.94 thousand/mm^3). Enlisted groundcrew had the highest mean WBC count (6.91 thousand/mm^3), followed by enlisted flyers (6.80 thousand/mm^3), then officers (6.33 thousand/mm^3). The current cigarette smoking and lifetime cigarette smoking history associations were positive ($r=0.395$ and $r=0.236$, respectively), indicating WBC count increased as the level of current cigarette smoking and the level of lifetime cigarette smoking history increased.

Analysis of WBC count in its discrete form revealed significant associations with race ($p=0.001$), current cigarette smoking ($p=0.001$), and lifetime cigarette smoking history ($p=0.001$), and a marginally significant association with occupation ($p=0.056$). Blacks displayed a higher percentage of abnormally low WBC counts (18.8%) than did non-Blacks (4.5%), but a lower percentage of abnormally high WBC counts (2.3%) than non-Blacks (3.7%). Officers displayed the highest percentage of abnormally low WBC counts (6.1%), but the lowest percentage of abnormally high WBC counts (2.3%). Enlisted flyers had the lowest percentage of abnormally low WBC counts (4.7%), while also displaying the highest percentage of abnormally high WBC counts (5.3%). Participants who had never smoked displayed the highest percentage of abnormally low WBC count levels (7.9%). The percentage of abnormally low WBC counts decreased as current cigarette smoking levels increased. The converse was true for the percentage of abnormally high WBC count levels. Participants smoking more than 20 cigarettes per day had the highest percentage of abnormally high WBC counts (16.1%), while nonsmokers had the lowest (1.4%). The tests of association with lifetime cigarette smoking history were similar to current cigarette smoking. Participants who had never smoked had the highest percentage of abnormally low WBC counts (7.9%), while participants in the more than 10 pack-years category displayed the highest percentage of abnormally high WBC counts (5.3%).

Tests of associations with hemoglobin in its continuous form revealed significant results for age ($p<0.001$), race ($p<0.001$), and current cigarette smoking ($p<0.001$). The association with occupation was marginally significant ($p=0.076$). Hemoglobin levels decreased as age increased ($r=-0.137$). Non-Blacks had a higher hemoglobin mean (15.36 gm/dl) than Blacks (14.77 gm/dl), while the highest hemoglobin mean was found among enlisted groundcrew (15.37 gm/dl). Hemoglobin levels increased as current cigarette smoking levels increased ($r=0.213$).

Hemoglobin in its discrete form also showed significant associations with age ($p=0.002$), race ($p=0.001$), and current cigarette smoking ($p=0.031$). The percentage of abnormally low hemoglobin levels was higher among older participants (8.3%) than among younger participants (4.5%). Blacks displayed a higher percentage of abnormally low hemoglobin levels (17.2%) than non-Blacks (6.0%). Former cigarette smokers had the highest percentage of abnormally low hemoglobin levels (8.1%), whereas 2.2 percent of participants smoking more than an average of 20 cigarettes per day had abnormally low

hemoglobin levels. Participants who smoked no more than 20 cigarettes per day displayed the highest percentage of abnormally high hemoglobin levels (1.1%), while participants who had never smoked had the lowest percentage (0.3%).

Significant associations with hematocrit in its continuous form were observed for age ($p<0.001$), race ($p<0.001$), occupation ($p=0.050$), and current cigarette smoking ($p<0.001$). A marginally significant association was found with lifetime cigarette smoking history ($p=0.085$). Hematocrit levels decreased as age increased ($r=-0.121$). The mean level of hematocrit was 45.65 percent for non-Blacks, compared to 44.49 percent for Blacks. Within the occupational strata, mean levels of hematocrit were 45.38 percent, 45.62 percent, and 45.74 percent for officers, enlisted flyers, and enlisted groundcrew, respectively. Hematocrit levels increased as current cigarette smoking increased ($r=0.209$). Hematocrit levels increased as lifetime cigarette smoking levels increased ($r=0.037$).

Age was significantly associated with hematocrit in its discrete form ($p=0.014$). The percentage of abnormally low hematocrit levels was higher among older participants (3.2%) than among younger participants (1.3%). The percentage of abnormally high levels of hematocrit was 0.3 percent for older participants compared to 0.2 percent for younger participants.

Platelet count in its continuous form displayed significant associations with age ($p<0.001$), occupation ($p=0.015$), current cigarette smoking ($p=0.005$), and lifetime cigarette smoking history ($p<0.001$). Tests of association revealed that platelet count decreased as age increased ($r=-0.120$). Platelet count means were highest among enlisted groundcrew (208.2 thousand/mm^3), followed by enlisted flyers (205.5 thousand/mm^3), then officers (201.6 thousand/mm^3). Positive relations between platelet count and current cigarette smoking ($r=0.062$) and lifetime cigarette smoking history ($r=0.094$) indicated that platelet counts increased as the number of cigarettes per day and the number of pack-years increased, respectively.

Age was significantly associated with platelet count in its discrete form ($p=0.022$). Current cigarette smoking was marginally significantly associated with platelet count ($p=0.070$). The rate of abnormally low platelet counts was 3.7 percent among older participants and 1.9 percent among younger participants. The rate of abnormally high platelet counts was also higher among older participants (0.6%) than among younger participants (0.2%). Abnormally low platelet counts were most prevalent among participants who smoked no more than 20 cigarettes per day on average (3.4%). The highest percentage of abnormally high platelet counts was among participants smoking more than 20 cigarettes per day (2.2%).

Prothrombin time in its continuous form was significantly associated with age ($p<0.001$). Prothrombin time increased as age increased ($r=0.096$). The association was marginally significant between age and the discrete form of prothrombin time ($p=0.077$). A greater percentage of participants with abnormal (high) prothrombin times was observed in older participants (1.9%) than in younger participants (0.8%).

RBC morphology was significantly associated with age, race, current cigarette smoking, and lifetime cigarette smoking history ($p=0.013$, $p=0.001$, $p=0.001$, and $p=0.001$, respectively). The association between RBC morphology and occupation was marginally significant ($p=0.072$). Older participants and Blacks displayed the higher percentages of RBC morphology abnormalities (8.0% and 14.1%, respectively) as compared to younger participants and non-Blacks (5.2% and 6.3%, respectively). The RBC morphology abnormality rates increased as the levels of current cigarette smoking and lifetime cigarette smoking history each increased (3.7%, 7.3%, 9.7%, and 10.2% for the four current cigarette smoking categories and 3.7%, 7.0%, and 8.5% for the three lifetime cigarette smoking history categories). The percentages of abnormalities were 9.5 for enlisted flyers, 6.7 for enlisted groundcrew, and 5.8 for officers.

Examination of absolute neutrophils (segs) displayed significant covariate associations with race ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Mean absolute neutrophils (segs) levels were 3.88 thousand/mm^3 for non-Blacks and 3.13 thousand/mm^3 for Blacks. Within the occupational strata, mean absolute neutrophils (segs) levels were highest among enlisted groundcrew (4.00 thousand/mm^3), followed by enlisted flyers (3.94 thousand/mm^3), then officers (3.60 thousand/mm^3). Absolute neutrophils (segs) increased as current cigarette smoking and lifetime cigarette smoking increased ($r=0.347$ and $r=0.214$, respectively).

For participants with positive absolute neutrophil (bands) levels, significant covariate associations were seen with age ($p=0.003$), race ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). The level of absolute neutrophil (bands) increased as age, current cigarette smoking, and lifetime cigarette smoking history increased ($r=0.071$ for age, $r=0.188$, for current cigarette smoking; $r=0.133$ for lifetime cigarette smoking history). The significant absolute neutrophil (bands) association with race revealed a mean of 0.200 thousand/mm^3 for non-Blacks and a mean of 0.120 thousand/mm^3 for Blacks. A significant association with race also was revealed when the percentage of participants with measurements of zero absolute neutrophils (bands) was examined ($p=0.032$). For Blacks, 24.2 percent had zero absolute neutrophils, whereas 16.5 percent of non-Blacks had zero absolute neutrophils.

Absolute lymphocytes were significantly associated with age ($p<0.001$), race ($p=0.035$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p=0.002$). Absolute lymphocyte levels decreased as age increased ($r=-0.116$). Blacks displayed higher mean absolute lymphocyte levels (1.87 thousand/mm^3) than did non-Blacks (1.75 thousand/mm^3). Mean levels of absolute lymphocytes for each occupational stratum were 1.82 thousand/mm^3 for enlisted groundcrew, 1.75 thousand/mm^3 for enlisted flyers, and 1.68 thousand/mm^3 for officers. Absolute lymphocyte levels increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.195$ and $r=0.067$, respectively).

Results from the examination of covariate associations for absolute monocytes revealed significant associations with age ($p=0.043$), current cigarette smoking ($p<0.001$), and lifetime cigarette smoking history ($p<0.001$). Absolute monocyte levels increased as each of these covariates increased ($r=0.044$ for age, $r=0.160$ for current cigarette smoking, and $r=0.142$ for lifetime cigarette smoking history).

For participants with positive absolute eosinophil levels, significant associations were found between current cigarette smoking and lifetime cigarette smoking history ($p<0.001$ for each). Absolute eosinophils increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.134$ and $r=0.086$, respectively). The percentage of participants with zero eosinophils was significantly associated with occupation ($p=0.005$). The percentages of participants with zero eosinophils were 14.7 for enlisted groundcrew, 11.5 for enlisted flyers, and 9.7 for officers.

Race, current cigarette smoking, and lifetime cigarette smoking history were significantly associated with basophils ($p=0.006$, $p<0.001$, and $p<0.001$, respectively) for participants whose absolute basophil level was positive. Mean levels of absolute basophils were 0.080 thousand/mm^3 for non-Blacks, compared to 0.068 thousand/mm^3 for Blacks. Basophils increased as current cigarette smoking and lifetime cigarette smoking history increased ($r=0.267$ and $r=0.168$, respectively). The proportion of participants with zero basophils was significantly associated with current cigarette smoking and lifetime cigarette smoking history ($p=0.033$ and $p=0.038$, respectively). Among levels of current cigarette smoking, the two highest percentages of participants with zero basophils were among participants who had never smoked (59.2%) and participants who were currently the heaviest smokers (59.9%). The percentage of participants with zero basophils decreased as the level of lifetime cigarette smoking history increased.

15.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 15-1. Dependent variables are derived from the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 15-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 parts per trillion (ppt). If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin is included in this model to account for body-fat-related differences in elimination rate (40).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used in determining the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used in determining the dioxin level.

15.2.2.1 Laboratory Examination Variables

15.2.2.1.1 RBC Count (Continuous)

The Model 3 unadjusted analysis of dioxin categories revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons. The mean RBC count was higher for Comparisons than for Ranch Hands in the low dioxin category (Table 15-3(e): p=0.094, difference of adjusted means=–0.05 million/mm^3). Other analyses of dioxin categories in Model 3 and analyses from Models 1, 2, and 4 were all nonsignificant (Table 15-3(a–h): p>0.10 for all other analyses).

Table 15-3. Analysis of RBC Count (million/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***4.95***	***–0.02 (–0.05,0.02)***	***0.318***
	Comparison	***1,249***	***4.96***		
Officer	Ranch Hand	341	4.89	–0.03 (–0.09,0.02)	0.234
	Comparison	493	4.92		
Enlisted Flyer	Ranch Hand	151	4.92	–0.04 (–0.12,0.04)	0.333
	Comparison	187	4.97		
Enlisted Groundcrew	Ranch Hand	374	5.01	0.01 (–0.04,0.06)	0.753
	Comparison	569	5.00		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***4.95***	***–0.02 (–0.05,0.02)***	***0.311***
	Comparison	***1,248***	***4.96***		
Officer	Ranch Hand	340	4.91	–0.03 (–0.08,0.02)	0.268
	Comparison	493	4.94		
Enlisted Flyer	Ranch Hand	151	4.94	–0.04 (–0.12,0.04)	0.343
	Comparison	187	4.98		
Enlisted Groundcrew	Ranch Hand	373	4.98	0.00 (–0.05,0.05)	0.919
	Comparison	568	4.97		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean[a]	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	4.91	4.91	0.019	0.023 (0.014)	0.102
Medium	162	4.97	4.97			
High	156	4.99	4.99			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-3. Analysis of RBC Count (million/mm^3) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	4.96	0.070	–0.004 (0.016)	0.821
Medium	162	4.98			
High	156	4.96			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	4.96	4.96		
Background RH	381	4.94	4.95	–0.01 (–0.06,0.03)	0.540
Low RH	239	4.92	4.92	–0.05 (–0.10,0.01)	0.094
High RH	239	4.99	4.98	0.02 (–0.04,0.07)	0.506
Low plus High RH	478	4.96	4.95	–0.01 (–0.05,0.03)	0.510

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	4.97		
Background RH	380	4.97	0.00 (–0.04,0.05)	0.893
Low RH	238	4.93	–0.03 (–0.09,0.02)	0.230
High RH	239	4.94	–0.02 (–0.08,0.03)	0.441
Low plus High RH	477	4.94	–0.03 (–0.07,0.01)	0.196

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-3. Analysis of RBC Count (million/mm^3) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	4.94	0.003	0.013 (0.009)	0.136
Medium	287	4.92			
High	284	4.99			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean**	**R^2**	**Adjusted Slope (Std. Error)**	**p-Value**
Low	287	4.99	0.047	–0.001 (0.010)	0.941
Medium	286	4.96			
High	284	4.98			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.2 RBC Count (Discrete)

All results from the analyses of RBC count in the discrete form were nonsignificant (Table 15-4(a–h): p>0.15 for each unadjusted and adjusted analysis of Models 1 through 4).

Table 15-4. Analysis of RBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***866***	***42 (4.9)***	***818 (94.5)***	***6 (0.7)***	***1.01 (0.67,1.51)***	***0.979***	***0.62 (0.24,1.61)***	***0.322***
	Comparison	***1,249***	***60 (4.8)***	***1,175 (94.1)***	***14 (1.1)***				
Officer	Ranch Hand	341	19 (5.6)	321 (94.1)	1 (0.3)	0.97 (0.53,1.77)	0.921	0.24 (0.03,1.98)	0.185
	Comparison	493	28 (5.7)	459 (93.1)	6 (1.2)				
Enlisted Flyer	Ranch Hand	151	11 (7.3)	138 (91.4)	2 (1.3)	2.03 (0.77,5.36)	0.155	1.29 (0.18,9.27)	0.800
	Comparison	187	7 (3.7)	178 (95.2)	2 (1.1)				
Enlisted Groundcrew	Ranch Hand	374	12 (3.2)	359 (96.0)	3 (0.8)	0.72 (0.36,1.45)	0.357	0.75 (0.19,3.02)	0.685
	Comparison	569	25 (4.4)	538 (94.6)	6 (1.1)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***1.00 (0.66,1.51)***	***0.991***	***0.58 (0.22,1.54)***	***0.278***
Officer	0.95 (0.52,1.75)	0.869	0.23 (0.03,1.89)	0.170
Enlisted Flyer	1.97 (0.73,5.29)	0.180	1.25 (0.17,9.24)	0.830
Enlisted Groundcrew	0.75 (0.37,1.53)	0.426	0.73 (0.18,2.98)	0.660

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%) Abnormal Low	Normal	Abnormal High	Analysis Results for Log_2 (Initial Dioxin)[a] Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[b]	p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	9 (5.6)	150 (93.8)	1 (0.6)	0.79 (0.53,1.15)	0.220	0.76 (0.36,1.59)	0.464
Medium	162	7 (4.3)	151 (93.2)	4 (2.5)				
High	156	5 (3.2)	151 (96.8)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.95 (0.64, 1.41)	0.804	0.88 (0.39, 1.99)	0.751

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high RBC count.

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	55 (4.5)	1,142 (94.3)	14 (1.2)				
Background RH	381	19 (5.0)	361 (94.8)	1 (0.3)	1.09 (0.64,1.87)	0.757	0.26 (0.03,1.99)	0.195
Low RH	239	12 (5.0)	225 (94.1)	2 (0.8)	1.11 (0.58,2.10)	0.753	0.69 (0.15,3.06)	0.623
High RH	239	9 (3.8)	227 (95.0)	3 (1.3)	0.83 (0.40,1.70)	0.603	0.94 (0.26,3.33)	0.921
Low plus High RH	478	21 (4.4)	452 (94.6)	5 (1.1)	0.96 (0.57,1.61)	0.868	0.80 (0.28,2.30)	0.683

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.07 (0.61,1.86)	0.818	0.25 (0.03,1.99)	0.192
Low RH	238	0.92 (0.48,1.78)	0.809	0.54 (0.12,2.48)	0.431
High RH	239	1.04 (0.49,2.23)	0.917	1.16 (0.31,4.42)	0.827
Low plus High RH	477	0.98 (0.57,1.68)	0.942	0.79 (0.27,2.33)	0.676

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-4. Analysis of RBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category	n	1987 Dioxin Category Summary Statistics Number (%) Abnormal Low	Normal	Abnormal High	Analysis Results for Log_2 (1987 Dioxin + 1) Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	13 (4.5)	274 (95.1)	1 (0.4)	0.91 (0.73,1.14)	0.405	1.16 (0.69,1.95)	0.566
Medium	287	16 (5.6)	270 (94.1)	1 (0.4)				
High	284	11 (3.9)	269 (94.7)	4 (1.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (1987 Dioxin + 1) Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.91 (0.69,1.21)	0.511	1.10 (0.60,2.00)	0.764

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.3 WBC Count (Continuous)

Each Model 1 contrast examining WBC count differences between Ranch Hands and Comparison means was nonsignificant, with and without covariate adjustment (Table 15-5(a,b): p>0.35 for each contrast).

Table 15-5. Analysis of WBC Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***6.67***	***0.02 --***	***0.789***
	Comparison	***1,249***	***6.65***		
Officer	Ranch Hand	341	6.33	0.00 --	0.970
	Comparison	493	6.33		
Enlisted Flyer	Ranch Hand	151	6.72	–0.14 --	0.474
	Comparison	187	6.86		
Enlisted Groundcrew	Ranch Hand	374	6.97	0.11 --	0.358
	Comparison	569	6.86		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***6.26***	***0.00 --***	***0.974***
	Comparison	***1,248***	***6.26***		
Officer	Ranch Hand	340	6.03	0.00 --	0.972
	Comparison	493	6.03		
Enlisted Flyer	Ranch Hand	151	6.17	–0.14 --	0.377
	Comparison	187	6.31		
Enlisted Groundcrew	Ranch Hand	373	6.55	0.05 --	0.648
	Comparison	568	6.50		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-5. Analysis of WBC Count (thousand/mm^3) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	6.48	6.50	0.022	0.019 (0.009)	0.035
Medium	162	6.91	6.92			
High	156	6.90	6.88			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of WBC count versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	6.08	0.213	0.008 (0.009)	0.414
Medium	162	6.29			
High	156	6.22			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	6.64	6.64		
Background RH	381	6.53	6.57	–0.07 --	0.493
Low RH	239	6.57	6.56	–0.08 --	0.491
High RH	239	6.96	6.92	0.28 --	0.029
Low plus High RH	478	6.76	6.73	0.09 --	0.324

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-5. Analysis of WBC Count (thousand/mm^3) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	6.27		
Background RH	380	6.28	0.01 --	0.902
Low RH	238	6.18	–0.09 --	0.383
High RH	239	6.33	0.06 --	0.600
Low plus High RH	477	6.26	–0.01 --	0.831

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	6.45	0.007	0.015 (0.006)	0.013
Medium	287	6.60			
High	284	6.95			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	6.09	0.219	0.007 (0.006)	0.263
Medium	286	6.18			
High	284	6.32			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of WBC count versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis of WBC count revealed a significant positive association between WBC count in its continuous form and initial dioxin (Table 15-5(c): p=0.035, slope=0.019). After covariate adjustment, the relation was nonsignificant (Table 15-5(d): p=0.414).

The mean WBC count for Ranch Hands in the high dioxin category was significantly greater than Comparisons in the Model 3 unadjusted analysis of WBC count (Table 15-5(e): p=0.029, difference of adjusted means=0.28 thousand/mm^3). Other unadjusted contrasts were nonsignificant, as well as all contrasts in the adjusted analysis (Table 15-5(e,f): p>0.32 for all other contrasts).

A significant positive association between WBC count and 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 15-5(g): p=0.013, slope=0.015). The association was nonsignificant after adjustment for covariates (Table 15-5(h): p=0.263).

15.2.2.1.4 WBC Count (Discrete)

No significant differences were found between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (Table 15-6(a,b): p≥0.15 for each contrast).

Both the unadjusted and adjusted Model 2 analyses revealed a significant inverse association between initial dioxin and abnormally low WBC counts (Table 15-6(c,d): p=0.012, Est. RR=0.59; p=0.043, Adj. RR=0.61, respectively). As initial dioxin increased, the percentage of abnormally low WBC counts decreased. Analyses of the associations between initial dioxin and the percentage of participants with abnormally high WBC counts were nonsignificant (Table 15-6(c,d): p>0.39 for each analysis).

A higher percentage of abnormally low WBC counts was found among Ranch Hands in the low dioxin category relative to Comparisons (Table 15-6(e): p=0.027, Est. RR=1.82). After adjustment for covariates, this result became marginally significant (Table 15-6(f): p=0.070, Adj. RR=1.67). No other differences in the percentage of abnormal WBC counts between Ranch Hands and Comparisons were found (Table 15-6(e,f): p>0.18 for each remaining contrast).

Table 15-6. Analysis of WBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***866***	***51 (5.9)***	***784 (90.5)***	***31 (3.6)***	***1.20 (0.82,1.75)***	***0.353***	***1.00 (0.63,1.60)***	***0.988***
	Comparison	***1,249***	***62 (5.0)***	***1,142 (91.4)***	***45 (3.6)***				
Officer	Ranch Hand	341	22 (6.5)	312 (91.5)	7 (2.1)	1.10 (0.62,1.95)	0.747	0.85 (0.33,2.17)	0.727
	Comparison	493	29 (5.9)	452 (91.7)	12 (2.4)				
Enlisted Flyer	Ranch Hand	151	10 (6.6)	133 (88.1)	8 (5.3)	2.14 (0.76,6.05)	0.150	1.03 (0.40,2.68)	0.954
	Comparison	187	6 (3.2)	171 (91.4)	10 (5.4)				
Enlisted Groundcrew	Ranch Hand	374	19 (5.1)	339 (90.6)	16 (4.3)	1.08 (0.59,1.97)	0.809	1.07 (0.55,2.05)	0.850
	Comparison	569	27 (4.8)	519 (91.2)	23 (4.0)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***1.18 (0.80,1.74)***	***0.415***	***0.93 (0.58,1.51)***	***0.783***
Officer	1.10 (0.62,1.96)	0.754	0.91 (0.35,2.35)	0.843
Enlisted Flyer	2.12 (0.73,6.09)	0.165	0.99 (0.37,2.68)	0.985
Enlisted Groundcrew	1.03 (0.55,1.93)	0.923	0.93 (0.47,1.82)	0.822

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	16 (10.0)	139 (86.9)	5 (3.1)	0.59 (0.39,0.89)	0.012	0.99 (0.69,1.43)	0.964
Medium	162	7 (4.3)	148 (91.4)	7 (4.3)				
High	156	3 (1.9)	147 (94.2)	6 (3.9)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.61 (0.38,0.99)	0.043	0.83 (0.54,1.27)	0.395

[a] Relative risk for a twofold increase in initial dioxin.

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	59 (4.9)	1,109 (91.6)	43 (3.6)				
Background RH	381	25 (6.6)	344 (90.3)	12 (3.2)	1.22 (0.75,1.99)	0.426	0.86 (0.45,1.67)	0.664
Low RH	239	20 (8.4)	212 (88.7)	7 (2.9)	1.82 (1.07,3.10)	0.027	0.86 (0.38,1.94)	0.716
High RH	239	6 (2.5)	222 (92.9)	11 (4.6)	0.56 (0.24,1.32)	0.188	1.32 (0.67,2.61)	0.420
Low plus High RH	478	26 (5.4)	434 (90.8)	18 (3.8)	1.01 (0.59,1.73)	0.963	1.07 (0.60,1.89)	0.825

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210				
Background RH	380	1.16 (0.70,1.93)	0.564	0.86 (0.43,1.71)	0.660
Low RH	238	1.67 (0.96,2.91)	0.070	0.82 (0.36,1.90)	0.650
High RH	239	0.64 (0.26,1.56)	0.326	1.09 (0.53,2.24)	0.825
Low plus High RH	477	1.03 (0.59,1.81)	0.907	0.95 (0.52,1.72)	0.855

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-6. Analysis of WBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	19 (6.6)	261 (90.6)	8 (2.8)	0.78 (0.63,0.96)	0.020	0.99 (0.77,1.27)	0.957
Medium	287	24 (8.4)	254 (88.5)	9 (3.1)				
High	284	8 (2.8)	263 (92.6)	13 (4.6)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.76 (0.59,0.98)	0.032	0.93 (0.72,1.20)	0.570

[a] Relative risk for a twofold increase in 1987 dioxin.

Although the contrasts of Ranch Hands in the low dioxin category and Comparisons indicated an increased percentage of Ranch Hands with an abnormally low WBC count (8.4% vs. 4.9%), contrasts of Ranch Hands in the high dioxin category and Comparisons showed the opposite pattern. As shown in Table 15-6(e) and 15-6(f), a smaller percentage of Ranch Hands in the high dioxin category (2.5%) had an abnormally low WBC count than did Comparisons (4.9%). Because of these opposite patterns, the percentages of Ranch Hands in the low and high dioxin categories combined and Comparisons were nearly equal. Consequently, a dose-response pattern was not evident between abnormally low WBC counts and dioxin in the Model 3 analyses.

Similar to the Model 2 analysis, the Model 4 unadjusted analysis of WBC count displayed a significant inverse relation between 1987 dioxin levels and abnormally low WBC count (Table 15-6(g): p=0.020, Est. RR=0.78). The significant relation remained after adjustment for covariates (Table 15-6(h): p=0.032, Adj. RR=0.76). As 1987 dioxin increased, the percentage of abnormally low WBC counts decreased. The associations between abnormally high WBC counts and 1987 dioxin were nonsignificant (Table 15-6(g,h): p≥0.57 for the unadjusted and adjusted analyses).

15.2.2.1.5 Hemoglobin (Continuous)

No significant results were found in the Model 1 unadjusted and adjusted analyses of hemoglobin in its continuous form (Table 15-7(a,b): p>0.20 for all contrasts).

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***15.32***	***0.00 (–0.09,0.09)***	***0.979***
	Comparison	***1,249***	***15.33***		
Officer	Ranch Hand	341	15.23	–0.06 (–0.20,0.08)	0.389
	Comparison	493	15.29		
Enlisted Flyer	Ranch Hand	151	15.29	–0.08 (–0.30,0.13)	0.445
	Comparison	187	15.38		
Enlisted Groundcrew	Ranch Hand	374	15.42	0.09 (–0.05,0.22)	0.206
	Comparison	569	15.34		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***15.05***	***–0.01 (–0.09,0.08)***	***0.883***
	Comparison	***1,248***	***15.05***		
Officer	Ranch Hand	340	15.03	–0.05 (–0.18,0.09)	0.489
	Comparison	493	15.07		
Enlisted Flyer	Ranch Hand	151	15.02	–0.09 (–0.29,0.12)	0.422
	Comparison	187	15.10		
Enlisted Groundcrew	Ranch Hand	373	15.07	0.06 (–0.07,0.19)	0.356
	Comparison	568	15.01		

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	15.21	15.21	0.011	0.078 (0.034)	0.023
Medium	162	15.34	15.34			
High	156	15.52	15.52			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	15.10	0.084	0.030 (0.039)	0.443
Medium	162	15.16			
High	156	15.28			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	15.33	15.33		
Background RH	381	15.31	15.30	–0.03 (–0.14,0.09)	0.641
Low RH	239	15.26	15.26	–0.07 (–0.21,0.07)	0.319
High RH	239	15.45	15.46	0.12 (–0.01,0.26)	0.080
Low plus High RH	478	15.36	15.36	0.03 (–0.08,0.13)	0.617

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-7. Analysis of Hemoglobin (gm/dl) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,210	15.06		
Background RH	380	15.04	–0.02 (–0.14,0.09)	0.679
Low RH	238	15.04	–0.02 (–0.16,0.11)	0.731
High RH	239	15.12	0.06 (–0.08,0.20)	0.379
Low plus High RH	477	15.08	0.02 (–0.08,0.12)	0.715

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean	R^2	Slope (Std. Error)	p-Value
Low	288	15.34	0.003	0.035 (0.023)	0.133
Medium	287	15.22			
High	284	15.45			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	15.13	0.088	0.021 (0.026)	0.421
Medium	286	15.06			
High	284	15.19			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant positive association between hemoglobin and initial dioxin was found in the unadjusted Model 2 analysis (Table 15-7(c): p=0.023, slope=0.078). The association was nonsignificant after adjustment for covariates (Table 15-7(d): p=0.443).

The Model 3 unadjusted analysis revealed a marginally significant higher mean hemoglobin level for Ranch Hands in the high dioxin category than for Comparisons (Table 15-7(e): p=0.080, difference of adjusted means=0.12 gm/dl). All other unadjusted contrasts were nonsignificant (Table 15-7(e): p>0.31 for all other contrasts). The contrast between Ranch Hands in the high dioxin category and Comparisons, as well as all other adjusted analysis contrasts, was nonsignificant (Table 15-7(f): p>0.37 for all adjusted contrasts).

The unadjusted and adjusted Model 4 analyses of hemoglobin revealed no significant associations with dioxin (Table 15-7(g,h): $p>0.13$ for both analyses).

15.2.2.1.6 Hemoglobin (Discrete)

Model 1 and Model 3 analyses of hemoglobin in its discrete form found no significant difference between Ranch Hands and Comparisons with respect to hemoglobin abnormalities (Table 15-8(a,b,e,f): $p>0.11$ for each unadjusted and adjusted contrast).

The Model 2 unadjusted analysis of hemoglobin revealed a marginally significant inverse association between initial dioxin and abnormally low hemoglobin levels (Table 15-8(c): $p=0.075$, Est. RR=0.74). After adjustment for covariates, the association was nonsignificant (Table 15-8(d): $p=0.364$). The association between abnormally high hemoglobin levels and initial dioxin was nonsignificant for both unadjusted and adjusted analyses (Table 15-8(c,d): $p>0.85$ for both analyses).

Table 15-8. Analysis of Hemoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
			Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***62 (7.2)***	***801 (92.5)***	***3 (0.4)***	***1.14 (0.81,1.61)***	***0.458***	***0.62 (0.16,2.41)***	***0.493***
	Comparison	***1,249***	***79 (6.3)***	***1,163 (93.1)***	***7 (0.6)***				
Officer	Ranch Hand	341	25 (7.3)	314 (92.1)	2 (0.6)	1.27 (0.73,2.21)	0.400	1.47 (0.21,10.49)	0.700
	Comparison	493	29 (5.9)	462 (93.7)	2 (0.4)				
Enlisted Flyer	Ranch Hand	151	16 (10.6)	134 (88.7)	1 (0.7)	1.60 (0.74,3.44)	0.230	--	0.899[a]
	Comparison	187	13 (7.0)	174 (93.1)	0 (0.0)				
Enlisted Groundcrew	Ranch Hand	374	21 (5.6)	353 (94.4)	0 (0.0)	0.85 (0.49,1.47)	0.557	--	0.171[a]
	Comparison	569	37 (6.5)	527 (92.6)	5 (0.9)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hemoglobin level.

--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***1.15 (0.81,1.63)***	***0.433***	***0.61 (0.16,2.38)***	***0.480***
Officer	1.25 (0.72,2.19)	0.433	1.52 (0.21,10.95)	0.675
Enlisted Flyer	1.58 (0.73,3.44)	0.246	--	--
Enlisted Groundcrew	0.90 (0.51,1.58)	0.713	--	--

--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high hemoglobin level.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	13 (8.1)	147 (91.9)	0 (0.0)	0.74 (0.53,1.03)	0.075	1.16 (0.24,5.60)	0.856
Medium	162	11 (6.8)	150 (92.6)	1 (0.6)				
High	156	5 (3.2)	151 (96.8)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	0.85 (0.61,1.20)	0.364	1.04 (0.17,6.53)	0.966

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation or race because of the sparse number of participants with an abnormal high hemoglobin level.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	74 (6.1)	1,130 (93.3)	7 (0.6)				
Background RH	381	30 (7.9)	349 (91.6)	2 (0.5)	1.35 (0.86,2.10)	0.188	1.04 (0.21,5.12)	0.958
Low RH	239	16 (6.7)	223 (93.3)	0 (0.0)	1.09 (0.62,1.90)	0.767	--	0.507[c]
High RH	239	13 (5.4)	225 (94.1)	1 (0.4)	0.86 (0.47,1.58)	0.630	0.64 (0.08,5.28)	0.677
Low plus High RH	478	29 (6.1)	448 (93.7)	1 (0.2)	0.97 (0.62,1.51)	0.887	--	0.547[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hemoglobin level.
--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal High vs. Normal: p-Value
Comparison	1,210				
Background RH	380	1.44 (0.91,2.29)	0.118	1.01 (0.20,5.14)	0.987
Low RH	238	0.96 (0.54,1.70)	0.886	--	--
High RH	239	0.90 (0.48,1.69)	0.735	0.69 (0.08,6.00)	0.735
Low plus High RH	477	0.93 (0.59,1.47)	0.746	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal high hemoglobin level.

Note: RH = Ranch Hand. Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt. Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with an abnormal high hemoglobin level.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category	n	1987 Dioxin Category Summary Statistics Number (%): Abnormal Low	Normal	Abnormal High	Analysis Results for Log_2 (1987 Dioxin + 1): Abnormal Low vs. Normal: Est. Relative Risk (95% C.I.)[a]	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Est. Relative Risk (95% C.I.)[a]	Abnormal High vs. Normal: p-Value
Low	288	21 (7.3)	265 (92.0)	2 (0.7)	0.82 (0.68,1.00)	0.049	0.47 (0.20,1.14)	0.096
Medium	287	23 (8.0)	264 (92.0)	0 (0.0)				
High	284	15 (5.3)	268 (94.4)	1 (0.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-8. Analysis of Hemoglobin (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.84 (0.68,1.04)	0.108	0.52 (0.22,1.23)	0.135

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation or race because of the sparse number of participants with an abnormal high hemoglobin level.

The Model 4 unadjusted analysis revealed a significant inverse association between abnormally low hemoglobin levels and 1987 dioxin levels (Table 15-8(g): p=0.049, Est. RR=0.82). In addition, a marginally significant inverse association between abnormally high hemoglobin levels and 1987 dioxin levels was found in the unadjusted analysis (Table 15-8(g): p=0.096, Est. RR=0.47). After adjustment for covariates, the association became nonsignificant (p>0.10 for each analysis).

15.2.2.1.7 Hematocrit (Continuous)

The Model 2 analysis of hematocrit in its continuous form revealed a significant positive association between hemoglobin and initial dioxin (Table 15-9(c): p=0.021, slope=0.241). After adjustment for covariates, the relation was nonsignificant (Table 15-9(d): p=0.443). All other analyses were nonsignificant (Table 15-9(a–h): p>0.14 for all other analyses).

Table 15-9. Analysis of Hematocrit (percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***45.56***	***–0.04 (–0.31,0.24)***	***0.798***
	Comparison	***1,249***	***45.59***		
Officer	Ranch Hand	341	45.24	–0.24 (–0.67,0.19)	0.274
	Comparison	493	45.48		
Enlisted Flyer	Ranch Hand	151	45.49	–0.23 (–0.90,0.44)	0.504
	Comparison	187	45.72		
Enlisted Groundcrew	Ranch Hand	374	45.88	0.22 (–0.18,0.63)	0.279
	Comparison	569	45.65		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adj. Means (95% C.I.)	p-Value
All	***Ranch Hand***	***864***	***44.99***	***–0.06 (–0.32,0.21)***	***0.681***
	Comparison	***1,248***	***45.05***		
Officer	Ranch Hand	340	44.90	–0.21 (–0.63,0.21)	0.326
	Comparison	493	45.11		
Enlisted Flyer	Ranch Hand	151	44.92	–0.24 (–0.88,0.41)	0.477
	Comparison	187	45.16		
Enlisted Groundcrew	Ranch Hand	373	45.08	0.15 (–0.25,0.55)	0.457
	Comparison	568	44.93		

Table 15-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	160	45.17	45.17	0.011	0.241 (0.104)	0.021
Medium	162	45.58	45.58			
High	156	46.08	46.09			

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean	R^2	Adj. Slope (Std. Error)	p-Value
Low	159	45.06	0.068	0.091 (0.119)	0.443
Medium	162	45.26			
High	156	45.57			

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,211	45.61	45.61		
Background RH	381	45.57	45.56	–0.06 (–0.41,0.30)	0.756
Low RH	239	45.30	45.30	–0.31 (–0.74,0.12)	0.153
High RH	239	45.92	45.93	0.32 (–0.11,0.75)	0.147
Low plus High RH	478	45.61	45.61	0.00 (–0.32,0.33)	0.987

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,210	45.08		
Background RH	380	45.04	–0.04 (–0.39,0.32)	0.839
Low RH	238	44.87	–0.21 (–0.63,0.20)	0.318
High RH	239	45.22	0.14 (–0.29,0.56)	0.534
Low plus High RH	477	45.04	–0.04 (–0.36,0.28)	0.817

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)**		
1987 Dioxin	**n**	**Mean**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	288	45.68	0.001	0.077 (0.071)	0.278
Medium	287	45.20			
High	284	45.89			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	287	45.40	0.075	0.029 (0.079)	0.712
Medium	286	45.01			
High	284	45.42			

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.8 Hematocrit (Discrete)

Analyses of hematocrit in its discrete form revealed no significant differences for Models 1 through 4 (Table 15-10(a–h): p>0.24 for each analysis performed).

Table 15-10. Analysis of Hematocrit (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
			Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Occupational Category	Group	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***21 (2.4)***	***844 (97.5)***	***1 (0.1)***	***1.04 (0.59,1.84)***	***0.886***	***0.29 (0.03,2.47)***	***0.256***
	Comparison	***1,249***	***29 (2.3)***	***1,215 (97.3)***	***5 (0.4)***				
Officer	Ranch Hand	341	8 (2.4)	333 (97.7)	0 (0.0)	0.96 (0.39,2.37)	0.928	--	0.647[a]
	Comparison	493	12 (2.4)	479 (97.2)	2 (0.4)				
Enlisted Flyer	Ranch Hand	151	6 (4.0)	144 (95.4)	1 (0.7)	1.91 (0.53,6.88)	0.325	--	0.907[a]
	Comparison	187	4 (2.1)	183 (97.9)	0 (0.0)				
Enlisted Groundcrew	Ranch Hand	374	7 (1.9)	367 (98.1)	0 (0.0)	0.81 (0.32,2.05)	0.659	--	0.413[a]
	Comparison	569	13 (2.3)	553 (97.2)	3 (0.5)				

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hematocrit level.

--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal		Abnormal High vs. Normal	
	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value
All	***1.04 (0.59,1.85)***	***0.886***	***0.28 (0.03,2.40)***	***0.245***
Officer	0.95 (0.38,2.36)	0.908	--	--
Enlisted Flyer	1.84 (0.51,6.72)	0.353	--	--
Enlisted Groundcrew	0.85 (0.33,2.18)	0.739	--	--

--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high hematocrit level.

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	160	3 (1.9)	157 (98.1)	0 (0.0)	0.95 (0.58,1.57)	0.840	1.17 (0.24,5.66)	0.841
Medium	162	5 (3.1)	156 (96.3)	1 (0.6)				
High	156	2 (1.3)	154 (98.7)	0 (0.0)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
477	1.10 (0.66,1.85)	0.714	1.07 (0.17,6.61)	0.942

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race or occupation because of the sparse number of participants with an abnormal high hematocrit level.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	27 (2.2)	1,179 (97.4)	5 (0.4)				
Background RH	381	8 (2.1)	373 (97.9)	0 (0.0)	0.97 (0.43,2.16)	0.933	--	0.464[c]
Low RH	239	5 (2.1)	234 (97.9)	0 (0.0)	0.93 (0.35,2.43)	0.875	--	0.695[c]
High RH	239	5 (2.1)	233 (97.5)	1 (0.4)	0.91 (0.35,2.40)	0.850	0.91 (0.10,7.96)	0.931
Low plus High RH	478	10 (2.1)	467 (97.7)	1 (0.2)	0.92 (0.44,1.92)	0.820	--	0.856[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high hematocrit level
--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal Low vs. Normal: p-Value	Abnormal High vs. Normal: Adj. Relative Risk (95% C.I.)[a]	Abnormal High vs. Normal: p-Value
Comparison	1,210				
Background RH	380	1.00 (0.44,2.28)	0.998	--	--
Low RH	238	0.78 (0.29,2.07)	0.615	--	--
High RH	239	1.01 (0.37,2.77)	0.980	0.98 (0.10,9.53)	0.986
Low plus High RH	477	0.89 (0.42,1.89)	0.757	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal high hematocrit level.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race because of the sparse number of participants with an abnormal high hematocrit level.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category Summary Statistics		Number (%)			Analysis Results for Log_2 (1987 Dioxin + 1)			
					Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	7 (2.4)	281 (97.6)	0 (0.0)	0.91 (0.65,1.26)	0.568	1.41 (0.43,4.63)	0.573
Medium	287	4 (1.4)	283 (98.6)	0 (0.0)				
High	284	7 (2.5)	276 (97.2)	1 (0.4)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-10. Analysis of Hematocrit (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
857	0.97 (0.67,1.42)	0.894	1.44 (0.38,5.40)	0.588

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results not adjusted for race or occupation because of the sparse number of participants with an abnormal high hematocrit level.

15.2.2.1.9 Platelet Count (Continuous)

When Ranch Hands and Comparisons were examined across all occupations, the difference in mean platelet count between the groups was nonsignificant in both unadjusted and adjusted analyses (Table 15-11(a,b): $p \geq 0.15$ in both analyses). In both the unadjusted and adjusted analyses, significant differences in mean platelet counts were found between Ranch Hands and Comparisons within each occupational stratum (Table 15-11(a,b): $p \leq 0.014$ for all occupational strata in both unadjusted and adjusted analyses). Mean platelet counts were higher among Comparisons than among Ranch Hands for the officer stratum and higher among Ranch Hands than among Comparisons for the enlisted flyer and enlisted groundcrew strata.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***862***	***207.0***	***3.1 --***	***0.150***
	Comparison	***1,243***	***203.9***		
Officer	Ranch Hand	338	196.6	–8.5 --	0.012
	Comparison	490	205.1		
Enlisted Flyer	Ranch Hand	151	213.8	14.9 --	0.005
	Comparison	185	198.8		
Enlisted Groundcrew	Ranch Hand	373	213.9	9.3 --	0.004
	Comparison	568	204.6		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***860***	***205.8***	***2.9 --***	***0.172***
	Comparison	***1,242***	***203.0***		
Officer	Ranch Hand	337	199.1	–8.2 --	0.014
	Comparison	490	207.3		
Enlisted Flyer	Ranch Hand	151	213.3	15.6 --	0.003
	Comparison	185	197.7		
Enlisted Groundcrew	Ranch Hand	372	208.9	8.1 --	0.011
	Comparison	567	200.8		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	159	204.2	203.8	0.016	0.145 (0.057)	0.012
Medium	162	208.0	207.9			
High	155	217.8	218.2			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	158	207.5	0.090	0.073 (0.065)	0.262
Medium	162	207.6			
High	155	214.7			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,205	204.5	204.6		
Background RH	379	203.6	202.1	–2.5 --	0.374
Low RH	238	204.2	204.6	–0.1 --	0.987
High RH	238	215.7	217.2	12.6 --	<0.001
Low plus High RH	476	209.9	210.8	6.2 --	0.017

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-11. Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,204	204.2		
Background RH	378	202.3	–1.9 --	0.509
Low RH	237	204.4	0.2 --	0.959
High RH	238	214.8	10.6 --	0.002
Low plus High RH	475	209.6	5.4 --	0.038

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	288	203.1	0.009	0.109 (0.039)	0.005
Medium	284	203.9			
High	283	214.5			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	205.1	0.066	0.049 (0.044)	0.264
Medium	283	204.7			
High	283	209.1			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of platelet count versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 2 unadjusted analysis of platelet count in its continuous form revealed a significant positive association with initial dioxin (Table 15-11(c): p=0.012, slope=0.145). After adjustment for the effects of covariates, the association was nonsignificant (Table 15-11(d): p=0.262).

Unadjusted and adjusted Model 3 analyses of mean platelet count levels were significantly greater for Ranch Hands in the high dioxin category than for Comparisons (Table 15-11(e,f): difference of adjusted means=12.6 thousand/mm^3, p<0.001, for the unadjusted analysis; difference of adjusted means=10.6 thousand/mm^3, p=0.002, for the adjusted analysis). Mean platelet counts also were significantly greater for Ranch Hands in the low and high dioxin categories combined than for Comparisons (Table 15-11(e,f): difference of adjusted means=6.2 thousand/mm^3, p=0.017, for the unadjusted analysis; difference of adjusted means=5.4 thousand/mm^3, p=0.038, for the adjusted analysis). Although the mean difference increased as dioxin levels increased, other contrasts of Ranch Hands and Comparisons were nonsignificant (Table 15-11(e,f): p>0.37 for all remaining contrasts).

Similar to the Model 2 analysis, the Model 4 unadjusted analysis of platelet count in its continuous form revealed a significant positive association with the 1987 dioxin levels (Table 15-11(g): p=0.005, slope=0.109). The relation was nonsignificant after adjustment for covariates (Table 15-11(h): p=0.264).

15.2.2.1.10 Platelet Count (Discrete)

A significant difference in the percentage of participants with abnormally low platelet counts was observed between Ranch Hand and Comparison officers in both the unadjusted and adjusted analyses (Table 15-12(a,b): p=0.021, Est. RR=2.65; p=0.022, Adj. RR=2.64, respectively). A significant difference in the percentage of participants with abnormally low platelet counts also was found for enlisted flyers (Table 15-12(a,b): p=0.032, Est. RR=0.11; p=0.029, Adj. RR=0.10, for the unadjusted and adjusted analyses, respectively). More Ranch Hand than Comparison officers had abnormally low platelet counts, (4.7% vs. 1.8%), whereas more Comparison than Ranch Hand enlisted flyers exhibited abnormally low platelet counts (6.0 vs. 0.7%). Contrasts of all Ranch Hands versus all Comparisons, as well as Ranch Hand versus Comparison enlisted groundcrew, were nonsignificant (Table 15-12(a,b): p>0.11 for all contrasts).

No significant associations were seen between abnormal platelet counts and initial dioxin in the Model 2 analyses (p>0.15 for all analyses). The Model 3 contrasts of Ranch Hands in the high dioxin category with Comparisons revealed marginally significant differences, with a higher percentage of Comparisons having abnormal platelet counts (Table 15-12(e,f): p=0.067, Est. RR=0.26; p=0.068, Adj. RR=0.26, for the unadjusted and adjusted analyses, respectively). This same pattern was observed when Ranch Hands in the low and high categories combined were contrasted with Comparisons (Table 15-12(e,f): p=0.090, Est. RR=0.47; p=0.078, Adj. RR=0.45, for the unadjusted and adjusted analyses, respectively). All other Model 3 contrasts were nonsignificant (Table 15-12(e,f): p>0.21 for all remaining contrasts).

A significant association between 1987 dioxin levels and abnormally low platelet count measures was found in the Model 4 unadjusted analysis of platelet count (Table 15-12(g): p=0.028, Est. RR=0.70). These results were nonsignificant after adjustment for covariates (Table 15-12(h): p=0.135). Other analyses of abnormal platelet counts with 1987 dioxin were nonsignificant (Table 15-12(g,h): p>0.61 for all other analyses).

Table 15-12. Analysis of Platelet Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Est. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Est. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***Ranch Hand***	***862***	***23 (2.7)***	***835 (96.9)***	***4 (0.5)***	***0.85 (0.50,1.43)***	***0.533***	***1.15 (0.31,4.29)***	***0.837***
	Comparison	***1,243***	***39 (3.1)***	***1,199 (96.5)***	***5 (0.4)***				
Officer	Ranch Hand	338	16 (4.7)	321 (95.0)	1 (0.3)	2.65 (1.16,6.06)	0.021	0.50 (0.05,4.79)	0.545
	Comparison	490	9 (1.8)	478 (97.6)	3 (0.6)				
Enlisted Flyer	Ranch Hand	151	1 (0.7)	149 (98.7)	1 (0.7)	0.11 (0.01,0.83)	0.032	1.16 (0.07,18.72)	0.916
	Comparison	185	11 (6.0)	173 (93.5)	1 (0.5)				
Enlisted Groundcrew	Ranch Hand	373	6 (1.6)	365 (97.9)	2 (0.5)	0.47 (0.19,1.20)	0.115	3.00 (0.27,33.23)	0.370
	Comparison	568	19 (3.4)	548 (96.5)	1 (0.2)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Abnormal Low vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal Low vs. Normal p-Value	Abnormal High vs. Normal Adj. Relative Risk (95% C.I.)	Abnormal High vs. Normal p-Value
All	***0.84 (0.50,1.42)***	***0.509***	***1.13 (0.30,4.27)***	***0.853***
Officer	2.64 (1.15,6.05)	0.022	0.55 (0.06,5.37)	0.606
Enlisted Flyer	0.10 (0.01,0.79)	0.029	1.18 (0.07,19.42)	0.906
Enlisted Groundcrew	0.48 (0.19,1.23)	0.127	2.61 (0.23,29.36)	0.437

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	159	3 (1.9)	156 (98.1)	0 (0.0)	0.63 (0.33,1.19)	0.152	1.28 (0.49,3.36)	0.616
Medium	162	4 (2.5)	157 (96.9)	1 (0.6)				
High	155	1 (0.7)	153 (98.7)	1 (0.7)				

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
475	0.69 (0.35,1.37)	0.290	0.67 (0.16,2.88)	0.590

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and race because of the sparse number of participants with an abnormal high platelet count.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,205	35 (2.9)	1,165 (96.7)	5 (0.4)				
Background RH	379	14 (3.7)	363 (95.8)	2 (0.5)	1.40 (0.74,2.66)	0.299	1.02 (0.19,5.30)	0.984
Low RH	238	6 (2.5)	232 (97.5)	0 (0.0)	0.84 (0.35,2.03)	0.702	--	0.693[c]
High RH	238	2 (0.8)	234 (98.3)	2.(0.8)	0.26 (0.06,1.10)	0.067	2.61 (0.49,13.84)	0.261
Low plus High RH	476	8 (1.7)	466 (97.9)	2 (0.4)	0.47 (0.20,1.13)	0.090	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal high platelet count.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,204				
Background RH	378	1.40 (0.73,2.70)	0.310	0.86 (0.16,4.61)	0.858
Low RH	237	0.79 (0.33,1.92)	0.604	--	--
High RH	238	0.26 (0.06,1.11)	0.068	3.37 (0.50,22.63)	0.211
Low plus High RH	475	0.45 (0.19,1.09)	0.078	--	--

[a] Relative risk and confidence interval relative to Comparisons.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin + 1)			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Est. Relative Risk (95% C.I.)[a]	p-Value	Est. Relative Risk (95% C.I.)[a]	p-Value
Low	288	10 (3.5)	276 (95.8)	2 (0.7)	0.70 (0.50,0.96)	0.028	0.95 (0.48,1.88)	0.879
Medium	284	8 (2.8)	276 (97.2)	0 (0.0)				
High	283	4 (1.4)	277 (97.9)	2 (0.7)				

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-12. Analysis of Platelet Count (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (1987 Dioxin + 1)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adj. Relative Risk (95% C.I.)[a]	p-Value	Adj. Relative Risk (95% C.I.)[a]	p-Value
853	0.73 (0.49,1.10)	0.135	0.84 (0.43,1.64)	0.619

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of participants with an abnormal high platelet count.

15.2.2.1.11 Prothrombin Time (Continuous)

All results from analyses of prothrombin time in its continuous form were nonsignificant for Models 1 through 4 (Table 15-13: $p \geq 0.22$ for all analyses).

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***688***	***10.48***	***–0.01 --***	***0.870***
	Comparison	***1,016***	***10.49***		
Officer	Ranch Hand	265	10.54	0.02 --	0.720
	Comparison	402	10.52		
Enlisted Flyer	Ranch Hand	114	10.46	–0.03 --	0.748
	Comparison	157	10.49		
Enlisted Groundcrew	Ranch Hand	309	10.45	–0.02 --	0.714
	Comparison	457	10.47		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***687***	***10.49***	***–0.01 --***	***0.873***
	Comparison	***1,015***	***10.50***		
Officer	Ranch Hand	265	10.52	0.02 --	0.765
	Comparison	402	10.50		
Enlisted Flyer	Ranch Hand	114	10.45	–0.03 --	0.718
	Comparison	157	10.48		
Enlisted Groundcrew	Ranch Hand	308	10.50	–0.02 --	0.762
	Comparison	456	10.51		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	119	10.47	10.48	0.004	–0.001 (0.003)	0.572
Medium	128	10.46	10.46			
High	128	10.45	10.44			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	119	10.48	0.036	0.000 (0.003)	0.956
Medium	128	10.50			
High	128	10.51			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	987	10.49	10.49		
Background RH	309	10.52	10.53	0.04 --	0.476
Low RH	182	10.47	10.46	–0.03 --	0.667
High RH	193	10.45	10.44	–0.05 --	0.411
Low plus High RH	375	10.46	10.45	–0.04 --	0.409

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-13. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	986	10.50		
Background RH	308	10.52	0.02 --	0.695
Low RH	182	10.46	–0.04 --	0.521
High RH	193	10.49	–0.01 --	0.823
Low plus High RH	375	10.47	–0.03 --	0.575

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	235	10.51	0.002	–0.002 (0.002)	0.220
Medium	218	10.50			
High	231	10.45			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	234	10.50	0.016	–0.001 (0.002)	0.685
Medium	218	10.50			
High	231	10.50			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of prothrombin time versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.12 Prothrombin Time (Discrete)

All results from analyses of prothrombin time in its discrete form were nonsignificant for Models 1 through 4 (Table 15-14: p>0.29 for all analyses).

Table 15-14. Analysis of Prothrombin Time (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***688***	***10 (1.5)***	***1.14 (0.50,2.61)***	***0.761***
	Comparison	***1,016***	***13 (1.3)***		
Officer	Ranch Hand	265	6 (2.3)	1.31 (0.43,3.93)	0.634
	Comparison	402	7 (1.7)		
Enlisted Flyer	Ranch Hand	114	0 (0.0)	--	0.999[a]
	Comparison	157	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	309	4 (1.3)	1.19 (0.32,4.45)	0.801
	Comparison	457	5 (1.1)		

[a] P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a high prothrombin time.
--: Results not presented because of the sparse number of participants with a high prothrombin time.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.13 (0.49,2.60)***	***0.781***
Officer	1.29 (0.43,3.91)	0.650
Enlisted Flyer	--	--
Enlisted Groundcrew	1.15 (0.30,4.35)	0.838

--: Results not presented because of the sparse number of participants with a high prothrombin time.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	119	2 (1.7)	0.66 (0.28,1.58)	0.315
Medium	128	1 (0.8)		
High	128	1 (0.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-14. Analysis of Prothrombin Time (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
375	0.72 (0.28,1.85)	0.470

[a] Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and current cigarette smoking because of the sparse number of participants with a high prothrombin time.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	987	13 (1.3)		
Background RH	309	6 (1.9)	1.64 (0.61,4.37)	0.327
Low RH	182	3 (1.7)	1.17 (0.33,4.19)	0.807
High RH	193	1 (0.5)	0.34 (0.04,2.62)	0.297
Low plus High RH	375	4 (1.1)	0.62 (0.17,2.23)	0.461

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	986		
Background RH	308	1.41 (0.52,3.85)	0.501
Low RH	182	1.01 (0.28,3.71)	0.984
High RH	193	0.49 (0.06,3.96)	0.502
Low plus High RH	375	0.70 (0.19,2.57)	0.586

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-14. Analysis of Prothrombin Time (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) High	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	235	3 (1.3)	0.86 (0.55,1.34)	0.498
Medium	218	6 (2.8)		
High	231	1 (0.4)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
683	0.86 (0.54, 1.38)	0.526

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with a high prothrombin time.

15.2.2.1.13 RBC Morphology

The Model 3 unadjusted analysis revealed a marginally significant difference in RBC morphology between Ranch Hands in the low dioxin category and Comparisons (Table 15-15(e): p=0.051, Est. RR=1.63). After adjustment for covariates, the result was nonsignificant (Table 15-15(f): p=0.206). All results from other analyses of RBC morphology also were nonsignificant (Table 15-15(a–h): p>0.19 for all other analyses).

Table 15-15. Analysis of RBC Morphology

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Abnormal	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***64 (7.4)***	***1.18 (0.84,1.66)***	***0.339***
	Comparison	***1,249***	***79 (6.3)***		
Officer	Ranch Hand	341	20 (5.9)	1.03 (0.57,1.87)	0.910
	Comparison	493	28 (5.7)		
Enlisted Flyer	Ranch Hand	151	15 (9.9)	1.10 (0.53,2.29)	0.793
	Comparison	187	17 (9.1)		
Enlisted Groundcrew	Ranch Hand	374	29 (7.8)	1.32 (0.79,2.21)	0.286
	Comparison	569	34 (6.0)		

Table 15-15. Analysis of RBC Morphology (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***1.16 (0.82,1.64)***	***0.400***
Officer	1.03 (0.57,1.87)	0.923
Enlisted Flyer	1.09 (0.52,2.30)	0.814
Enlisted Groundcrew	1.31 (0.78,2.22)	0.307

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	14 (8.8)	0.94 (0.73,1.21)	0.622
Medium	162	16 (9.9)		
High	156	9 (5.8)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
477	1.02 (0.76,1.38)	0.878

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED				
Dioxin Category	**n**	**Number (%) Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,211	73 (6.0)		
Background RH	381	24 (6.3)	1.12 (0.69,1.81)	0.639
Low RH	239	23 (9.6)	1.63 (1.00,2.67)	0.051
High RH	239	16 (6.7)	1.05 (0.60,1.85)	0.862
Low plus High RH	478	39 (8.2)	1.31 (0.87,1.98)	0.196

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-15. Analysis of RBC Morphology (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.18 (0.72,1.93)	0.517
Low RH	238	1.39 (0.84,2.30)	0.206
High RH	239	1.08 (0.60,1.94)	0.800
Low plus High RH	477	1.22 (0.80,1.86)	0.352

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Abnormal	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	20 (6.9)	1.03 (0.87,1.23)	0.698
Medium	287	25 (8.7)		
High	284	18 (6.3)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	1.02 (0.84,1.25)	0.822

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.14 Absolute Neutrophils (Segs)

All Model 1 and 2 results from the analyses of absolute neutrophils (segs) were nonsignificant (Table 15-16(a–d): p>0.11 for each analysis).

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***3.84***	***0.03 --***	***0.612***
	Comparison	***1,249***	***3.81***		
Officer	Ranch Hand	341	3.59	–0.02 --	0.804
	Comparison	493	3.61		
Enlisted Flyer	Ranch Hand	151	3.92	–0.02 --	0.885
	Comparison	187	3.95		
Enlisted Groundcrew	Ranch Hand	374	4.06	0.10 --	0.263
	Comparison	569	3.95		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***3.46***	***0.01 --***	***0.774***
	Comparison	***1,248***	***3.45***		
Officer	Ranch Hand	340	3.26	–0.02 --	0.808
	Comparison	493	3.28		
Enlisted Flyer	Ranch Hand	151	3.44	–0.03 --	0.804
	Comparison	187	3.47		
Enlisted Groundcrew	Ranch Hand	373	3.68	0.06 --	0.416
	Comparison	568	3.61		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	3.77	3.78	0.015	0.019 (0.012)	0.115
Medium	162	4.00	4.00			
High	156	4.02	4.00			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	3.37	0.198	0.000 (0.012)	0.988
Medium	162	3.43			
High	156	3.38			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	3.82	3.81		
Background RH	381	3.73	3.75	–0.06 --	0.430
Low RH	239	3.81	3.80	–0.01 --	0.906
High RH	239	4.05	4.03	0.22 --	0.028
Low plus High RH	478	3.93	3.91	0.10 --	0.172

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-16. Analysis of Absolute Neutrophils (segs) (thousand/mm^3) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	3.45		
Background RH	380	3.45	0.00 --	0.961
Low RH	238	3.44	–0.01 --	0.854
High RH	239	3.50	0.05 --	0.551
Low plus High RH	477	3.47	0.02 --	0.780

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	3.70	0.007	0.020 (0.008)	0.017
Medium	287	3.79			
High	284	4.04			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	3.39	0.196	0.006 (0.008)	0.455
Medium	286	3.42			
High	284	3.50			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (segs) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The Model 3 unadjusted analysis revealed a significantly higher absolute neutrophil mean for Ranch Hands in the high dioxin category than for Comparisons (Table 15-16(e): p=0.028, difference of adjusted means=0.22 thousand/mm^3). After adjustment for covariates, the difference was nonsignificant (Table 15-16(f): p=0.551). All other Model 3 analyses also were nonsignificant (Table 15-16(e,f): p>0.17 for remaining Model 3 analyses).

A significant positive association between 1987 dioxin levels and absolute neutrophils was revealed from the Model 4 unadjusted analysis (Table 15-16(g): p=0.017, slope=0.020). The association became nonsignificant after adjustment for covariate effects (Table 15-16(h): p=0.455).

15.2.2.1.15 Absolute Neutrophils (Bands) (Nonzero Measurements)

For participants who had a positive number of absolute neutrophils (bands), the unadjusted and adjusted Model 1 analyses revealed a marginally significant difference in absolute neutrophil means between Ranch Hand and Comparison enlisted groundcrew (Table 15-17(a,b): difference of means=0.021 thousand/mm^3, p=0.089; difference of adjusted means=0.016 thousand/mm^3, p=0.099, respectively). The Ranch Hand absolute neutrophil mean was greater than the Comparison mean. All other Model 1 contrasts were nonsignificant (Table 15-17(a,b): p>0.12 for each remaining contrast).

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***720***	***0.201***	***0.012 --***	***0.123***
	Comparison	***1,037***	***0.189***		
Officer	Ranch Hand	294	0.194	0.014 --	0.250
	Comparison	406	0.180		
Enlisted Flyer	Ranch Hand	115	0.190	–0.014 --	0.478
	Comparison	160	0.204		
Enlisted Groundcrew	Ranch Hand	311	0.213	0.021 --	0.089
	Comparison	471	0.193		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***718***	***0.159***	***0.009*** --	***0.126***
	Comparison	***1,036***	***0.150***		
Officer	Ranch Hand	293	0.152	0.011 --	0.221
	Comparison	406	0.141		
Enlisted Flyer	Ranch Hand	115	0.143	–0.013 --	0.389
	Comparison	160	0.156		
Enlisted Groundcrew	Ranch Hand	310	0.177	0.016 --	0.099
	Comparison	470	0.161		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	131	0.194	0.195	0.004	–0.031 (0.032)	0.343
Medium	132	0.249	0.250			
High	134	0.195	0.194			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	130	0.146	0.117	–0.075 (0.036)	0.040
Medium	132	0.174			
High	134	0.132			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,002	0.189	0.189		
Background RH	316	0.189	0.191	0.002 --	0.783
Low RH	196	0.212	0.211	0.022 --	0.079
High RH	201	0.211	0.209	0.020 --	0.113
Low plus High RH	397	0.211	0.210	0.021 --	0.029

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,001	0.148		
Background RH	315	0.150	0.002 --	0.750
Low RH	195	0.165	0.017 --	0.076
High RH	201	0.161	0.013 --	0.166
Low plus High RH	396	0.163	0.015 --	0.038

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-17. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	241	0.184	0.001	0.015 (0.021)	0.482
Medium	233	0.204			
High	239	0.217			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	240	0.136	0.076	0.011 (0.024)	0.657
Medium	232	0.154			
High	239	0.164			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus $\log_2$ (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

A significant negative association between initial dioxin and absolute neutrophils (bands) was found in the Model 2 adjusted analysis (Table 15-17(d): p=0.040, adjusted slope=–0.075). Results were nonsignificant in the unadjusted analysis (Table 15-17(c): p=0.343).

The Model 3 contrast of Ranch Hands in the low dioxin category with Comparisons revealed a marginally significant difference of means, indicating a higher absolute neutrophil mean among Ranch Hands than Comparisons (Table 15(e,f): difference of adjusted means=0.022 thousand/mm^3, p=0.079; difference of adjusted means=0.017 thousand/mm^3, p=0.076, for the unadjusted and adjusted analyses, respectively). Similarly, the mean difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was significant (Table 15-17(e,f): p=0.029, difference of adjusted means=0.021 thousand/mm^3; p=0.038, difference of adjusted means=0.015 thousand/mm^3, for the unadjusted and adjusted analyses, respectively). All other Model 3 contrasts and each analysis performed from Model 4 were nonsignificant (Table 15-17(e-h): p>0.11 for each remaining contrast).

15.2.2.1.16 Absolute Neutrophils (Bands) (Zero versus Nonzero)

Unadjusted and adjusted Model 1 analyses of the percentage of participants with no absolute neutrophils revealed a significant difference between Ranch Hand and Comparison enlisted flyers (Table 15-18(a,b): p=0.029, Est. RR=1.86; p=0.026, Adj. RR=1.88, for the unadjusted and adjusted analyses, respectively). A greater percentage of Ranch Hand than Comparison enlisted flyers had no absolute neutrophils (23.8% vs. 14.4%). All other Model 1 results and all results from the analyses of Models 2 through 4 were nonsignificant (Table 15-18(a–h): p>0.13 for all remaining analyses).

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Zero**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***866***	***146 (16.9)***	***0.99 (0.79,1.25)***	***0.945***
	Comparison	***1,249***	***212 (17.0)***		
Officer	Ranch Hand	341	47 (13.8)	0.75 (0.51,1.10)	0.136
	Comparison	493	87 (17.7)		
Enlisted Flyer	Ranch Hand	151	36 (23.8)	1.86 (1.07,3.23)	0.029
	Comparison	187	27 (14.4)		
Enlisted Groundcrew	Ranch Hand	374	63 (16.8)	0.97 (0.69,1.38)	0.880
	Comparison	569	98 (17.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED		
Occupational Category	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	***0.99 (0.79,1.25)***	***0.956***
Officer	0.74 (0.51,1.09)	0.134
Enlisted Flyer	1.88 (1.08,3.27)	0.026
Enlisted Groundcrew	0.98 (0.69,1.39)	0.918

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Number (%) Zero**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	160	29 (18.1)	0.92 (0.76,1.11)	0.381
Medium	162	30 (18.5)		
High	156	22 (14.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
477	0.87 (0.70,1.09)	0.214

[a] Relative risk for a twofold increase in initial dioxin.

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	209 (17.3)		
Background RH	381	65 (17.1)	0.98 (0.72,1.34)	0.908
Low RH	239	43 (18.0)	1.05 (0.73,1.51)	0.781
High RH	239	38 (15.9)	0.91 (0.62,1.33)	0.625
Low plus High RH	478	81 (17.0)	0.98 (0.74,1.30)	0.881

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.02 (0.75,1.40)	0.897
Low RH	238	1.03 (0.72,1.49)	0.859
High RH	239	0.88 (0.59,1.30)	0.515
Low plus High RH	477	0.95 (0.72,1.27)	0.741

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	47 (16.3)	0.99 (0.88,1.12)	0.905
Medium	287	54 (18.8)		
High	284	45 (15.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 15-18. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.92 (0.80,1.06)	0.264

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.17 Absolute Lymphocytes

The unadjusted and adjusted Model 2 analyses of absolute lymphocytes revealed a marginally significant positive association between absolute lymphocytes and initial dioxin (Table 15-19(c,d): p=0.063, slope=0.023; p=0.087, adjusted slope=0.024, for the unadjusted and adjusted analyses, respectively). Both analyses showed an increase in absolute lymphocyte levels for increasing initial dioxin levels. Results from each of the analyses of Models 1, 3, and 4 were nonsignificant (Table 15-19(a,b, and e–h): p>0.23 for all analyses).

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***1.76***	***0.00 --***	***0.920***
	Comparison	***1,249***	***1.75***		
Officer	Ranch Hand	341	1.70	0.04 --	0.392
	Comparison	493	1.67		
Enlisted Flyer	Ranch Hand	151	1.71	–0.08 --	0.248
	Comparison	187	1.79		
Enlisted Groundcrew	Ranch Hand	374	1.83	0.01 --	0.891
	Comparison	569	1.82		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***1.79***	***0.00 --***	***0.964***
	Comparison	***1,248***	***1.79***		
Officer	Ranch Hand	340	1.80	0.05 --	0.259
	Comparison	493	1.75		
Enlisted Flyer	Ranch Hand	151	1.74	–0.08 --	0.236
	Comparison	187	1.82		
Enlisted Groundcrew	Ranch Hand	373	1.82	–0.01 --	0.781
	Comparison	568	1.83		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	1.68	1.69	0.021	0.023 (0.012)	0.063
Medium	162	1.75	1.75			
High	156	1.83	1.82			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	1.76	0.064	0.024 (0.014)	0.087
Medium	162	1.81			
High	156	1.88			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	1.75	1.75		
Background RH	381	1.75	1.77	0.02 --	0.671
Low RH	239	1.72	1.71	–0.04 --	0.383
High RH	239	1.79	1.78	0.03 --	0.575
Low plus High RH	478	1.75	1.74	–0.01 --	0.839

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	1.79		
Background RH	380	1.83	0.04 --	0.356
Low RH	238	1.77	–0.02 --	0.572
High RH	239	1.77	–0.02 --	0.572
Low plus High RH	477	1.77	–0.02 --	0.457

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-19. Analysis of Absolute Lymphocytes (thousand/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)[b]**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	288	1.71	0.002	0.009 (0.008)	0.239
Medium	287	1.76			
High	284	1.79			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	287	1.73	0.050	0.007 (0.009)	0.455
Medium	286	1.79			
High	284	1.79			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.18 Absolute Monocytes

The Model 4 unadjusted analysis of absolute monocytes revealed a marginally significant positive association with 1987 dioxin levels (Table 15-20(g): p=0.059, slope=0.007). This association was nonsignificant after adjustment for covariates (Table 15-20(h): p=0.125). All analysis results from Models 1 through 3 also were nonsignificant (Table 15-20(a–f): p>0.10 for all other analyses).

Table 15-20. Analysis of Absolute Monocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***866***	***0.477***	***–0.004 --***	***0.648***
	Comparison	***1,249***	***0.481***		
Officer	Ranch Hand	341	0.463	–0.008 --	0.594
	Comparison	493	0.471		
Enlisted Flyer	Ranch Hand	151	0.470	–0.037 --	0.118
	Comparison	187	0.507		
Enlisted Groundcrew	Ranch Hand	374	0.492	0.011 --	0.455
	Comparison	569	0.482		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***864***	***0.471***	***–0.006 --***	***0.544***
	Comparison	***1,248***	***0.476***		
Officer	Ranch Hand	340	0.461	–0.007 --	0.620
	Comparison	493	0.468		
Enlisted Flyer	Ranch Hand	151	0.452	–0.037 --	0.106
	Comparison	187	0.490		
Enlisted Groundcrew	Ranch Hand	373	0.489	0.008 --	0.590
	Comparison	568	0.481		

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Table 15-20. Analysis of Absolute Monocytes (thousand/mm^3) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	160	0.468	0.469	0.003	0.003 (0.006)	0.568
Medium	162	0.528	0.528			
High	156	0.472	0.470			

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	159	0.463	0.041	0.000 (0.006)	0.999
Medium	162	0.508			
High	156	0.446			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,211	0.480	0.480		
Background RH	381	0.459	0.464	–0.016 --	0.221
Low RH	239	0.470	0.469	–0.011 --	0.480
High RH	239	0.508	0.502	0.022 --	0.136
Low plus High RH	478	0.489	0.486	0.006 --	0.606

[a] Transformed from square root scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-20. Analysis of Absolute Monocytes (thousand/mm^3) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,210	0.479		
Background RH	380	0.464	–0.015 --	0.223
Low RH	238	0.464	–0.015 --	0.319
High RH	239	0.499	0.020 --	0.193
Low plus High RH	477	0.482	0.003 --	0.822

[a] Transformed from square root scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c] P-value is based on difference of means on square root scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	288	0.458	0.004	0.007 (0.004)	0.059
Medium	287	0.467			
High	284	0.503			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	287	0.450	0.032	0.007 (0.004)	0.125
Medium	286	0.458			
High	284	0.493			

[a] Transformed from square root scale.
[b] Slope and standard error based on square root of absolute monocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.19 Absolute Eosinophils (Nonzero Measurements)

For participants who had a positive number of absolute eosinophils, all analyses in Models 1 through 4 were nonsignificant (Table 15-21(a–h): p>0.10 for all analyses).

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***760***	***0.159***	***–0.002 --***	***0.684***
	Comparison	***1,096***	***0.161***		
Officer	Ranch Hand	305	0.160	0.007 --	0.422
	Comparison	448	0.153		
Enlisted Flyer	Ranch Hand	134	0.162	–0.002 --	0.895
	Comparison	165	0.164		
Enlisted Groundcrew	Ranch Hand	321	0.157	–0.011 --	0.183
	Comparison	483	0.167		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***758***	***0.151***	***–0.003 --***	***0.576***
	Comparison	***1,095***	***0.154***		
Officer	Ranch Hand	304	0.154	0.007 --	0.347
	Comparison	448	0.147		
Enlisted Flyer	Ranch Hand	134	0.150	–0.003 --	0.806
	Comparison	165	0.153		
Enlisted Groundcrew	Ranch Hand	320	0.149	–0.013 --	0.106
	Comparison	482	0.162		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	139	0.155	0.155	0.001	0.005 (0.025)	0.836
Medium	144	0.154	0.154			
High	134	0.157	0.157			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	138	0.151	0.009	0.012 (0.029)	0.670
Medium	144	0.150			
High	134	0.155			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,064	0.161	0.161		
Background RH	337	0.162	0.163	0.002 --	0.805
Low RH	206	0.156	0.155	–0.006 --	0.513
High RH	211	0.155	0.154	–0.007 --	0.434
Low plus High RH	417	0.155	0.155	–0.006 --	0.346

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,063	0.153		
Background RH	336	0.156	0.003 --	0.677
Low RH	205	0.147	–0.006 --	0.447
High RH	211	0.144	–0.009 --	0.229
Low plus High RH	416	0.146	–0.007 --	0.194

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-21. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)[b]		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	256	0.164	0.001	–0.017 (0.017)	0.330
Medium	250	0.156			
High	248	0.155			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	255	0.156	0.028	–0.010 (0.020)	0.608
Medium	249	0.149			
High	248	0.148			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute eosinophils versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.20 Absolute Eosinophils (Zero versus Nonzero)

The percentage of participants with no absolute eosinophils present was not significantly associated with exposure group or dioxin in any of the Model 1 through 4 analyses (Table 15-22(a–h): p>0.37 for all analyses).

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***106 (12.2)***	***1.00 (0.77,1.30)***	***0.995***
	Comparison	***1,249***	***153 (12.3)***		
Officer	Ranch Hand	341	36 (10.6)	1.18 (0.74,1.86)	0.493
	Comparison	493	45 (9.1)		
Enlisted Flyer	Ranch Hand	151	17 (11.3)	0.95 (0.49,1.86)	0.885
	Comparison	187	22 (11.8)		
Enlisted Groundcrew	Ranch Hand	374	53 (14.2)	0.93 (0.64,1.34)	0.689
	Comparison	569	86 (15.1)		

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.01 (0.77,1.31)***	***0.970***
Officer	1.18 (0.74,1.87)	0.489
Enlisted Flyer	0.95 (0.49,1.87)	0.893
Enlisted Groundcrew	0.92 (0.64,1.34)	0.674

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	21 (13.1)	0.95 (0.77,1.17)	0.630
Medium	162	18 (11.1)		
High	156	22 (14.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.92 (0.73,1.18)	0.521

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	147 (12.1)		
Background RH	381	44 (11.6)	0.96 (0.67,1.38)	0.833
Low RH	239	33 (13.8)	1.15 (0.77,1.73)	0.487
High RH	239	28 (11.7)	0.95 (0.61,1.46)	0.798
Low plus High RH	478	61 (12.8)	1.04 (0.76,1.44)	0.789

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-22. Analysis of Absolute Eosinophils (Zero vs. Nonzero) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.07 (0.74,1.55)	0.705
Low RH	238	1.16 (0.77,1.76)	0.467
High RH	239	0.82 (0.53,1.27)	0.376
Low plus High RH	477	0.98 (0.71,1.35)	0.885

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	32 (11.1)	1.05 (0.91,1.20)	0.528
Medium	287	37 (12.9)		
High	284	36 (12.7)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin + 1)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.99 (0.84,1.16)	0.894

[a] Relative risk for a twofold increase in 1987 dioxin.

15.2.2.1.21 Absolute Basophils (Nonzero Measurements)

For participants who had a positive number of absolute basophils, no significant relations were observed between basophils and exposure group or dioxin in Model 1 through 4 analyses (Table 15-23(a–h): p>0.18 for each analysis).

Table 15-23. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***373***	***0.078***	***–0.002 --***	***0.315***
	Comparison	***580***	***0.080***		
Officer	Ranch Hand	149	0.076	–0.001 --	0.838
	Comparison	232	0.077		
Enlisted Flyer	Ranch Hand	75	0.079	–0.003 --	0.577
	Comparison	87	0.082		
Enlisted Groundcrew	Ranch Hand	149	0.079	–0.003 --	0.322
	Comparison	261	0.082		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***372***	***0.072***	***–0.002 --***	***0.280***
	Comparison	***580***	***0.074***		
Officer	Ranch Hand	148	0.071	–0.001 --	0.669
	Comparison	232	0.073		
Enlisted Flyer	Ranch Hand	75	0.072	–0.002 --	0.682
	Comparison	87	0.074		
Enlisted Groundcrew	Ranch Hand	149	0.073	–0.003 --	0.326
	Comparison	261	0.076		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 15-23. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	62	0.077	0.078	0.013	0.009 (0.022)	0.685
Medium	58	0.075	0.076			
High	81	0.081	0.080			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	61	0.073	0.082	–0.003 (0.026)	0.917
Medium	58	0.070			
High	81	0.073			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	562	0.080	0.080		
Background RH	168	0.077	0.078	–0.002 --	0.410
Low RH	92	0.076	0.076	–0.004 --	0.222
High RH	109	0.080	0.080	0.000 --	0.930
Low plus High RH	201	0.078	0.078	–0.002 --	0.482

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-23. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED				
Dioxin Category	**n**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]**	**p-Value[c]**
Comparison	562	0.075		
Background RH	168	0.074	–0.001 --	0.657
Low RH	91	0.071	–0.004 --	0.183
High RH	109	0.073	–0.002 --	0.563
Low plus High RH	200	0.072	–0.003 --	0.220

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin +1)[b]**		
1987 Dioxin	**n**	**Mean[a]**	**R^2**	**Slope (Std. Error)[b]**	**p-Value**
Low	132	0.076	<0.001	0.006 (0.014)	0.674
Medium	109	0.079			
High	128	0.078			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			**Analysis Results for Log_2 (1987 Dioxin + 1)**		
1987 Dioxin	**n**	**Adj. Mean[a]**	**R^2**	**Adjusted Slope (Std. Error)[b]**	**p-Value**
Low	132	0.069	0.076	–0.006 (0.016)	0.716
Medium	108	0.072			
High	128	0.067			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute basophils versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

15.2.2.1.22 Absolute Basophils (Zero versus Nonzero)

Unadjusted and adjusted Model 1 analyses of the percentage of participants with no absolute basophils revealed a significant difference between Ranch Hand and Comparison enlisted groundcrew (Table 15-24(a,b): p=0.068, Est. RR=1.28; p=0.065, Adj. RR=1.28, respectively). A greater percentage of

Ranch Hand than Comparison enlisted groundcrew had no absolute basophils. All other Model 1 contrasts were nonsignificant (Table 15-24(a,b): p>0.10 for each remaining contrast).

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Zero	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***866***	***493 (56.9)***	***1.15 (0.96,1.36)***	***0.126***
	Comparison	***1,249***	***669 (53.6)***		
Officer	Ranch Hand	341	192 (56.3)	1.15 (0.87,1.51)	0.338
	Comparison	493	261 (52.9)		
Enlisted Flyer	Ranch Hand	151	76 (50.3)	0.88 (0.57,1.35)	0.565
	Comparison	187	100 (53.5)		
Enlisted Groundcrew	Ranch Hand	374	225 (60.2)	1.28 (0.98,1.67)	0.068
	Comparison	569	308 (54.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1.16 (0.97,1.38)***	***0.106***
Officer	1.16 (0.88,1.53)	0.303
Enlisted Flyer	0.87 (0.57,1.34)	0.529
Enlisted Groundcrew	1.28 (0.98,1.68)	0.065

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	98 (61.3)	0.84 (0.73,0.97)	0.015
Medium	162	104 (64.2)		
High	156	75 (48.1)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
477	0.81 (0.68,0.95)	0.012

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,211	649 (53.6)		
Background RH	381	213 (55.9)	1.09 (0.86,1.38)	0.459
Low RH	239	147 (61.5)	1.39 (1.04,1.84)	0.025
High RH	239	130 (54.4)	1.04 (0.78,1.37)	0.796
Low plus High RH	478	277 (58.0)	1.20 (0.97,1.49)	0.098

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,210		
Background RH	380	1.11 (0.87,1.41)	0.395
Low RH	238	1.47 (1.10,1.95)	0.009
High RH	239	1.00 (0.75,1.33)	0.979
Low plus High RH	477	1.21 (0.97,1.50)	0.091

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 15-24. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)	
1987 Dioxin	n	Number (%) Zero	Estimated Relative Risk (95% C.I.)[a]	p-Value
Low	288	156 (54.2)	0.97 (0.88,1.06)	0.496
Medium	287	178 (62.0)		
High	284	156 (54.9)		

[a] Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
	Analysis Results for Log_2 (1987 Dioxin + 1)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
857	0.94 (0.84,1.05)	0.257

[a] Relative risk for a twofold increase in 1987 dioxin.

Model 2 analyses displayed a significant association between initial dioxin and the percentage of participants with no absolute basophils, both with and without adjustment for covariates (Table 15-24(c,d): p=0.015, Est. RR=0.84; p=0.012, Adj. RR=0.81, respectively). As initial dioxin increased, the percentage of participants with no absolute basophils decreased.

A significant difference in the proportion of participants with no absolute basophils was observed between Ranch Hands in the low dioxin category and Comparisons in both Model 3 unadjusted and adjusted analyses (Table 15-24(e,f): p=0.025, Est. RR=1.39; p=0.009, Adj. RR=1.47, respectively). Also, the contrast of Comparisons with Ranch Hands in the low and high dioxin categories combined was marginally significant in both the unadjusted and adjusted analyses (Table 15-24(e,f): p=0.098, Est. RR=1.20; p=0.091, Adj. RR=1.21, respectively). Ranch Hands in these dioxin categories had a higher percentage of participants with no absolute basophils than did Comparisons. All other Model 3 contrasts, as well as the Model 4 analysis results, were nonsignificant (Table 15-24(e–h): p>0.25 for all analyses).

15.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on platelet count to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin—the measure of exposure in these models—changes over time and is not available for all participants for 1982 or 1997.

Discrete and continuous analyses were performed for platelet count. The longitudinal analyses for these variables investigated the difference between the 1982 and 1997 examinations. These analyses were used to investigate the temporal effects of dioxin during the 15-year period between 1982 and 1997.

Participants who were abnormal in 1982 were not included in the longitudinal analysis of discrete dependent variables. The purpose of the longitudinal analysis was to examine the effects of dioxin exposure across time. Participants who were abnormal in 1982 were not considered to be at risk for developing the condition because the condition already existed at the time of the first collection of data for the AFHS (1982). Only participants considered normal at the 1982 examination were considered to be at risk for developing the condition; therefore, the rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (41). Summary statistics are provided for reference purposes for the 1985, 1987, and 1992 examinations.

The longitudinal analyses for platelet count in its discrete form examined relative risks at the 1997 examination for participants who were classified as normal at the 1982 examination. The adjusted relative risks estimated from each of the three models were used to investigate the change in the dependent variable over time. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

The longitudinal analysis for the platelet count in its continuous form examined the paired difference between the measurements from 1982 and 1997. These paired differences measured the change in platelet count over time. Each of the three models used in the longitudinal analysis was adjusted for age and platelet count as measured in 1982 (see Chapter 7, Statistical Methods). A square root transformation was applied to platelet count for analytic purposes.

15.2.3.1 Laboratory Variable

15.2.3.1.1 Platelet Count (Continuous)

A decrease was seen in both Ranch Hands and Comparison means between the baseline examination and the 1997 follow-up. The largest portion of the decrease was observed between 1992 and 1997. The change in platelet count means between 1982 and 1997 was examined for associations with group status and dioxin. In the Model 1 analysis, the change in platelet count means between 1982 and 1997 was significantly different between Ranch Hand and Comparison officers (Table 15-25(a): $p<0.001$). The difference was marginally significant in Ranch Hand and Comparison enlisted flyers (Table 15-25(a): $p=0.100$). For both occupations, Ranch Hands have decreased more than Comparisons over the 15-year time period. The difference was nonsignificant when Ranch Hands and Comparisons were examined across all occupations. No significant associations were observed between platelet count and dioxin in Model 2 (Table 15-25(b): $p=0.401$). In the Model 3 analysis, there was a marginally significant difference in the change in platelet count means between the background Ranch Hand dioxin category and Comparisons (Table 15-25(c)). The decrease in means between 1982 and 1997 was greater for Ranch Hands in the background dioxin category (66.0 thousand/mm^3) than for Comparisons (58.6 thousand/mm^3).

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***273.8 (807)***	***267.8 (788)***	***260.7 (779)***	***250.7 (782)***	***207.2 (807)***	***–66.6***	***–7.8***	***0.203***
	Comparison	***261.7 (966)***	***263.7 (946)***	***255.3 (937)***	***244.4 (944)***	***202.9 (966)***	***–58.8***		
Officer	Ranch Hand	262.4 (307)	258.3 (302)	252.0 (298)	239.3 (299)	196.9 (307)	–65.4	–13.5	<0.001
	Comparison	256.9 (376)	262.5 (370)	253.1 (362)	243.3 (370)	205.0 (376)	–51.9		
Enlisted Flyer	Ranch Hand	281.8 (147)	273.6 (144)	265.7 (142)	255.0 (144)	213.3 (147)	–68.5	–4.1	0.100
	Comparison	258.2 (143)	253.4 (142)	242.6 (141)	235.1 (140)	193.7 (143)	–64.4		
Enlisted Groundcrew	Ranch Hand	280.5 (353)	273.8 (342)	266.3 (339)	259.2 (339)	213.7 (353)	–66.7	–4.0	0.462
	Comparison	266.9 (447)	268.3 (434)	261.3 (434)	248.4 (434)	204.2 (447)	–62.7		

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of platelet count; results adjusted for square root of platelet count in 1982 and age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(b) MODEL 2: RANCH HANDS – INITIAL DIOXIN

Initial Dioxin Category Summary Statistics						Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination						
Initial Dioxin	1982	1985	1987	1992	1997	Adjusted Slope (Std. Error)	p-Value
Low	266.5 (152)	265.1 (148)	257.6 (150)	247.0 (147)	204.0 (152)	0.039 (0.046)	0.401
Medium	277.4 (159)	268.2 (156)	262.8 (155)	252.9 (155)	208.0 (159)		
High	284.9 (147)	274.8 (144)	268.5 (142)	259.6 (144)	217.6 (147)		

[a] Transformed from square root scale.
[b] Results based on difference between square root of 1997 platelet count and square root of 1982 platelet count versus log_2 (initial dioxin); results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 platelet count, and age in 1997.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

Table 15-25. Longitudinal Analysis of Platelet Count (thousand/mm^3) (Continuous) (Continued)

(c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Mean[a]/(n) Examination 1982	1985	1987	1992	1997	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	261.9 (938)	264.0 (921)	255.7 (911)	245.0 (917)	203.3 (938)	–58.6		
Background RH	270.3 (343)	265.2 (335)	257.5 (327)	247.4 (331)	204.3 (343)	–66.0	–7.4	0.071
Low RH	268.0 (228)	264.0 (221)	258.9 (223)	247.3 (220)	204.0 (228)	–64.0	–5.4	0.544
High RH	284.3 (230)	274.5 (227)	266.8 (224)	258.7 (226)	215.5 (230)	–68.8	–10.2	0.965
Low plus High RH	276.1 (458)	269.3 (448)	262.8 (447)	253.1 (446)	209.7 (458)	–66.4	–7.8	0.676

[a] Transformed from square root scale.
[b] Difference between 1997 and 1982 examination means after transformation to original scale.
[c] P-value is based on analysis of square root of 1997 platelet count; results adjusted for percent body fat at the date of the blood measurement of dioxin, square root of 1982 platelet count, and age in 1997.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations.

15.2.3.1.2 Platelet Count (Discrete)

The longitudinal analysis of 1997 platelet count in its discrete form was conditioned on participants who had a normal platelet count in 1982. In the Model 1 analyses, no significant difference was observed in the percentage of abnormally low platelet counts between Ranch Hands and Comparisons when all occupations were combined (Table 15-26(a1): p=0.681). Ranch Hand officers had a significantly higher percentage of abnormal low measurements than did Comparison officers (Table 15-26(a1): Adj. RR=2.71, p=0.046), and Ranch Hands enlisted flyers had a significantly smaller percentage of abnormal low measurements than did Comparison officers (Table 15-26(a1): Adj. RR=0.09, p=0.023). No significant differences were observed between Ranch Hands and Comparisons in the percentage of abnormally high measurements, although the sparse number of abnormally high measurements in 1997 precluded meaningful statistical analysis by occupation.

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal)

(a1) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal Low/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***2 (0.3)***	***1 (0.1)***	***0 (0.0)***	***3 (0.4)***	***21 (2.6)***
		807	***788***	***779***	***782***	***807***
	Comparison	***7 (0.7)***	***2 (0.2)***	***3 (0.3)***	***6 (0.6)***	***30 (3.1)***
		966	***946***	***937***	***944***	***966***
Officer	Ranch Hand	1 (0.3)	1 (0.3)	0 (0.0)	2 (0.7)	14 (4.6)
		307	302	298	299	307
	Comparison	3 (0.8)	0 (0.0)	0 (0.0)	3 (0.8)	7 (1.9)
		376	370	362	370	376
Enlisted Flyer	Ranch Hand	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
		147	144	142	144	147
	Comparison	0 (0.0)	1 (0.7)	2 (1.4)	1 (0.7)	10 (7.0)
		143	142	141	140	143
Enlisted Groundcrew	Ranch Hand	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)	6 (1.7)
		353	342	339	339	353
	Comparison	4 (0.9)	1 (0.2)	1 (0.2)	2 (0.5)	13 (2.9)
		447	434	434	434	447

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1997	Number (%) Abnormal Low in 1997		
All	***Ranch Hand***	***799***	***20 (2.5)***	***0.88 (0.49,1.59)***	***0.681***
	Comparison	***950***	***27 (2.8)***		
Officer	Ranch Hand	305	13 (4.3)	2.71 (1.02,7.23)	0.046
	Comparison	372	6 (1.6)		
Enlisted Flyer	Ranch Hand	146	1 (0.7)	0.09 (0.01,0.71)	0.023
	Comparison	141	10 (7.1)		
Enlisted Groundcrew	Ranch Hand	348	6 (1.7)	0.71 (0.26,1.94)	0.501
	Comparison	437	11 (2.5)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

(a2) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Number (%) Abnormal High/(n) Examination				
		1982	1985	1987	1992	1997
All	***Ranch Hand***	***6 (0.7)***	***12 (1.5)***	***16 (2.1)***	***9 (1.2)***	***4 (0.5)***
		807	***788***	***779***	***782***	***807***
	Comparison	***9 (0.9)***	***13 (1.4)***	***13 (1.4)***	***8 (0.9)***	***4 (0.4)***
		966	***946***	***937***	***944***	***966***
Officer	Ranch Hand	1 (0.3)	3 (1.0)	4 (1.3)	0 (0.0)	1 (0.3)
		307	302	298	299	307
	Comparison	1 (0.3)	3 (0.8)	5 (1.4)	3 (0.8)	3 (0.8)
		376	370	362	370	376
Enlisted Flyer	Ranch Hand	1 (0.7)	3 (2.1)	4 (2.8)	1 (0.7)	1 (0.7)
		147	144	142	144	147
	Comparison	2 (1.4)	3 (2.1)	1 (0.7)	2 (1.4)	1 (0.7)
		143	142	141	140	143
Enlisted Groundcrew	Ranch Hand	4 (1.1)	6 (1.8)	8 (2.4)	8 (2.4)	2 (0.6)
		353	342	339	339	353
	Comparison	6 (1.3)	7 (1.6)	7 (1.6)	3 (0.7)	0 (0.0)
		447	434	434	434	447

Occupational Category	Group	Normal in 1982		Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
		n in 1997	Number (%) Abnormal High in 1997		
All	***Ranch Hand***	***799***	***3 (0.4)***	***1.81 (0.30,10.89)***	***0.516***
	Comparison	***950***	***2 (0.2)***		
Officer	Ranch Hand	305	1 (0.3)	--	0.999[b]
	Comparison	372	2 (0.5)		
Enlisted Flyer	Ranch Hand	146	1 (0.7)	--	0.999[b]
	Comparison	141	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	348	1 (0.3)	--	0.912[b]
	Comparison	437	0 (0.0)		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

[b] P-value not presented because of the sparse number of participants with an abnormal high platelet count; results not adjusted for age in 1997.

--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

(b1) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Abnormal Low/(n) Examination				
Initial Dioxin	**1982**	**1985**	**1987**	**1992**	**1997**
Low	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (2.0)
	152	148	150	147	152
Medium	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.5)
	159	156	155	155	159
High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
	147	144	142	144	147

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	**n in 1997**	**Number (%) Abnormal Low in 1997**	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**
Low	150	2 (1.3)	0.83 (0.43,1.61)	0.586
Medium	158	4 (2.5)		
High	146	1 (0.7)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(b2) MODEL 2: RANCH HANDS — INITIAL DIOXIN

	Number (%) Abnormal High/(n) Examination				
Initial Dioxin	**1982**	**1985**	**1987**	**1992**	**1997**
Low	1 (0.7)	1 (0.7)	3 (2.0)	1 (0.7)	0 (0.0)
	152	148	150	147	152
Medium	1 (0.6)	2 (1.3)	4 (2.6)	3 (1.9)	1 (0.6)
	159	156	155	155	159
High	1 (0.7)	3 (2.1)	3 (2.1)	4 (2.8)	1 (0.7)
	147	144	142	144	147

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1997	Number (%) Abnormal High in 1997	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	150	0 (0.0)	1.28 (0.32,5.19)	0.726
Medium	158	1 (0.6)		
High	146	0 (0.0)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[b] Relative risk for a twofold increase in initial dioxin.

Notes: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(c1) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Abnormal Low/(n) Examination				
Dioxin Category	1982	1985	1987	1992	1997
Comparison	6 (0.6)	1 (0.1)	2 (0.2)	4 (0.4)	28 (3.0)
	938	921	911	917	938
Background RH	1 (0.3)	1 (0.3)	0 (0.0)	2 (0.6)	12 (3.5)
	343	335	327	331	343
Low RH	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	6 (2.6)
	228	221	223	220	228
High RH	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
	230	227	224	226	230
Low plus High RH	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	8 (1.8)
	458	448	447	446	458

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

	Normal in 1982			
Dioxin Category	**n in 1997**	**Number (%) Abnormal Low in 1997**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	923	26 (2.8)		
Background RH	339	12 (3.5)	1.33 (0.66,2.69)	0.424
Low RH	226	5 (2.2)	0.70 (0.26,1.85)	0.471
High RH	228	2 (0.9)	0.32 (0.07,1.36)	0.122
Low plus High RH	454	7 (1.5)	0.47 (0.19,1.18)	0.107

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

(c2) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Number (%) Abnormal High/(n) Examination				
Dioxin Category	**1982**	**1985**	**1987**	**1992**	**1997**
Comparison	9 (1.0)	13 (1.4)	13 (1.4)	8 (0.9)	4 (0.4)
	938	921	911	917	938
Background RH	3 (0.9)	5 (1.5)	6 (1.8)	1 (0.3)	2 (0.6)
	343	335	327	331	343
Low RH	1 (0.4)	2 (0.9)	4 (1.8)	2 (0.9)	0 (0.0)
	228	221	223	220	228
High RH	2 (0.9)	4 (1.8)	6 (2.7)	6 (2.7)	2 (0.9)
	230	227	224	226	230
Low plus High RH	3 (0.7)	6 (1.3)	10 (2.2)	8 (1.8)	2 (0.4)
	458	448	447	446	458

Table 15-26. Longitudinal Analysis of Platelet Count (Abnormal Low vs. Normal and Abnormal High vs. Normal) (Continued)

	Normal in 1982			
Dioxin Category	n in 1997	Number (%) Abnormal High in 1997	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	923	2 (0.2)		
Background RH	339	2 (0.6)	2.17 (0.30,15.65)	0.442
Low RH	226	0 (0.0)	--	0.999[c]
High RH	228	1 (0.4)	3.79 (0.32,45.31)	0.293
Low plus High RH	454	1 (0.2)	--	0.999[c]

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.
[c] P-value not presented because of the sparse number of participants with an abnormal high platelet count; results not adjusted for age in 1997.
--: Results not presented because of the sparse number of participants with an abnormal high platelet count.

Notes: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1985 are provided for reference purposes for participants who attended the 1982, 1985, and 1997 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the 1982, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1982, 1992, and 1997 examinations. Statistical analyses are based only on participants who had a normal platelet count in 1982 (see Chapter 7, Statistical Methods).

Model 2 analyses did not show a significant association of initial dioxin with either abnormally low or abnormally high platelet counts (Table 15-26(b1) and (b2): $p>0.58$ for each analysis). The Model 3 analyses of categorized dioxin also did not show any significant associations with abnormal platelet count levels (Table 15-26(c1) and (c2): $p>0.10$ for all analyses).

15.3 DISCUSSION

As indices of the three peripheral blood lines—RBCs, WBCs, and platelets—the hematologic variables analyzed are widely used in clinical medicine and are relied upon heavily to reflect disease not only of the hematopoietic system, but in other organ systems as well. Although lacking specificity, abnormalities in the hemoglobin, hematocrit, and total WBC count often serve as a sensitive first alert to the presence of a host of infection, inflammatory, and neoplastic disease states across multiple organ systems and point to the need for further investigation.

As elements essential to normal coagulation, the platelets have a short half-life and are most subject to decreased survival in a wide range of diseases, toxic chemical exposures, and in the presence of numerous over-the-counter and prescription medications. The broad range of normal for the platelet count (130 thousand/mm^3 to 400 thousand/mm^3) is such that subtle changes in platelet survival can occur and not be identified as abnormal. Only extreme variations in the platelet count—less than 50 thousand/mm^3 and

greater than 800 thousand/mm^3—are associated with the classic complications of spontaneous bleeding or blood clot formation.

Similar to the 1987 and 1992 examinations, most of the significant results were limited to the platelet and WBC analyses. Ranch Hand enlisted flyers and groundcrew had higher mean platelet counts than Comparisons, but the differences in the means (14.9 thousand/mm^3 and 9.3 thousand/mm^3, respectively) cannot be considered biologically meaningful.

Few of the serum dioxin analyses yielded significant results. In a pattern consistent with a dose-response effect, a positive association was noted between the mean platelet count and initial dioxin levels in the low, medium, and high categories. When adjusted for covariates, the associations were no longer significant. Similarly, in the model using 1987 dioxin levels, Ranch Hands with the highest levels of serum dioxin had significantly higher mean platelet counts than did Comparisons, but after adjustment for covariates, the association was not significant. Once again, the difference in the means was relatively small (never more than 14 thousand/mm^3). In the discrete analyses, which can be considered more relevant clinically, no significant group or occupational differences were noted, nor was there any evidence for a dioxin effect.

In the 1987 examinations, the mean WBC and platelet counts and the erythrocyte sedimentation rates were higher in Ranch Hands than Comparisons, raising the possibility of a subclinical inflammatory response associated with prior dioxin exposure. In the current study as in 1992, no significant group differences were noted in any of these indices. The unadjusted analyses of the WBC and platelet variables and, as noted in Chapter 9, of erythrocyte sedimentation rate, have yielded results consistent with a subtle dose-response effect in relation to both initial and 1987 dioxin levels. After adjustment for covariates, none of the findings remained significant.

Dependent variable-covariate associations confirmed numerous observations that have been well-established in clinical practice. In cigarette smokers, cellular hypoxia related to carboxyhemoglobin formation and systemic arterial desaturation in obstructive airway disease combine to raise the hemoglobin and hematocrit in comparison to nonsmokers. The increased incidence of chronic bronchitis in smokers is often associated with an elevation in the total WBC count. Of participants smoking at least one pack per day, 16.1 percent had abnormally elevated WBC counts, versus a prevalence of 1.4 percent in nonsmokers ($p=0.001$). Older participants were found to have statistically significant reductions in the total RBC, hemoglobin, and hematocrit associations that may reflect the increased incidence of chronic disease associated with age.

Race-related associations were noted. When compared to non-Black participants, Black participants had statistically significant reductions in the RBC indices, findings that may relate to the increased incidence of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency and of hemoglobin variants (S and C) associated with heterozygous sickling disorders. Blacks were found to have a greater prevalence of abnormally low RBC counts than non-Blacks (7.8% vs. 4.6%), although the difference in the means (4.99 thousand/mm^3 vs. 4.95 thousand/mm^3) is not statistically significant and is not likely clinically meaningful.

The longitudinal analyses documented a reduction in the total platelet count in each group and across all occupational strata. As documented in the 1987 follow-up report, Ranch Hands continue to have a greater reduction in the total platelet count over time than do Comparisons, although the current means (207.2 thousand/mm^3 vs. 202.9 thousand/mm^3) are nearly equal.

In conclusion, analyses of 13 hematologic variables yielded no significant group differences between the Ranch Hand and Comparison cohorts, and these results are consistent with the 1992 follow-up examination. In those participants most heavily exposed, the slight increase in the platelet count referenced above may still reflect a subtle biologic effect of dioxin exposure. Apart from platelet count, there appears to be little evidence to support a relation between dioxin exposure and adverse effects to the hematopoietic system.

15.4 SUMMARY

The hematology assessment included analyses of 13 variables each from the laboratory examination. For each variable, associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin (Model 4) were assessed. Continuous and discrete analyses were performed for each cell count variable as well as for prothrombin time. RBC morphology, as well as blood count variables, was also analyzed. In addition, due to the large number of nonzero measurements for absolute neutrophils (bands), absolute eosinophils, and absolute basophils, investigations on these variables consisted of two analyses. First, a discrete analysis was performed on the proportion of zero measurements, and second, a continuous analysis was performed on the nonzero measurements.

15.4.1 Model 1: Group Analysis

As shown in Table 15-27, in both the unadjusted and adjusted analyses of the cell count variables, only the analyses of platelet count revealed significant group differences. In the continuous analysis, group differences were significant for each occupation but not significant when examined across all occupations. The platelet count mean was higher for Comparison officers and higher for Ranch Hands in both enlisted flyers and enlisted groundcrew. In the discrete analysis of platelet count, unadjusted and adjusted results also revealed consistent results. Significant group differences in the percentage of abnormally low platelet counts were found within the officer and enlisted flyer strata. For officers, more Ranch Hands than Comparisons exhibited an abnormally low platelet count. Conversely, for enlisted flyers, more Comparisons than Ranch Hands had an abnormally low platelet count.

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	NS	ns	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	NS	ns	NS	NS
Hemoglobin (C)	NS	ns	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	NS	ns
Abnormal High vs. Normal	ns	NS	NS	ns

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Hematocrit (C)	ns	ns	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
Platelet Count (C)	NS	–0.012	+0.005	+0.004
Platelet Count (D)				
Abnormal Low vs. Normal	ns	+0.021	–0.032	ns
Abnormal High vs. Normal	NS	ns	NS	NS
Prothrombin Time (C)	ns	NS	ns	ns
Prothrombin Time (D)	NS	NS	ns	NS
RBC Morphology (D)	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	ns	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	ns	NS*
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	+0.029	ns
Absolute Lymphocytes (C)	NS	NS	ns	NS
Absolute Monocytes (C)	ns	ns	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	NS	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	ns	NS*

Note: NS*: Marginally significant ($0.05<p\leq0.10$).
NS or ns: Not significant ($p>0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 15-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	NS	ns	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	NS	NS
Abnormal High vs. Normal	ns	ns	ns	ns
Hemoglobin (C)	ns	ns	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	NS	ns
Abnormal High vs. Normal	ns	NS	--	--
Hematocrit (C)	ns	ns	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	--	--	--
Platelet Count (C)	NS	–0.014	+0.003	+0.011
Platelet Count (D)				
Abnormal Low vs. Normal	ns	+0.022	–0.029	ns
Abnormal High vs. Normal	NS	ns	NS	NS
Prothrombin Time (C)	ns	NS	ns	ns
Prothrombin Time (D)	NS	NS	--	NS
RBC Morphology (D)	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	ns	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	ns	NS*
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	+0.026	ns
Absolute Lymphocytes (C)	NS	NS	ns	ns
Absolute Monocytes (C)	ns	ns	ns	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	NS	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	ns	NS*

Note: NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
NS or ns: Not significant ($p>0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
–: Relative risk<1.00 for discrete analysis; difference of means negative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

The unadjusted and adjusted results from the analyses of the blood count variables also were similar. The continuous analyses of absolute neutrophils (bands) revealed a marginally significant higher mean for Ranch Hands within the enlisted groundcrew stratum. A greater percentage of zero measurements were found among Ranch Hand enlisted flyers than among Comparison enlisted flyers. For the analysis of absolute basophils, the difference in the proportions of zero measurements was marginally significant and higher for Ranch Hands than for Comparisons within the enlisted groundcrew stratum.

15.4.2 Model 2: Initial Dioxin Analysis

Unadjusted analyses of the cell count variables revealed several significant associations with initial dioxin, as shown in Table 15-28. The continuous analyses of WBC count, hemoglobin, hematocrit, and platelet count each showed a significant, positive relation with initial dioxin. After adjustment for covariate information, each association was nonsignificant. Other significant results include the discrete unadjusted and adjusted analyses of WBC count, revealing a decrease in the proportion of abnormally low WBC counts as initial dioxin increased.

Table 15-28. Summary of Initial Dioxin Analysis (Model 2) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	ns	ns
White Blood Cell (WBC) Count (C)	+0.035	NS
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	–0.012	–0.043
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	+0.023	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	ns*	ns
Abnormal High vs. Normal	NS	NS
Hematocrit (C)	+0.021	NS
Hematocrit (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	+0.012	NS
Platelet Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	ns
Prothrombin Time (C)	ns	NS
Prothrombin Time (D)	ns	ns
RBC Morphology	ns	NS
Absolute Neutrophils (Segs) (C)	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	ns	–0.040
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns

Table 15-28. Summary of Initial Dioxin Analysis (Model 2) for Hematology Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Absolute Lymphocytes (C)	NS*	NS*
Absolute Monocytes (C)	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	–0.015	–0.012

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis.
–: Relative risk<1.00; slope negative for continuous analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Among the blood count variables, the result from the unadjusted analysis of absolute neutrophils (bands) was nonsignificant. After adjustment for covariates, a significant negative association was revealed, where neutrophils decreased as initial dioxin increased. A marginally significant and positive association between initial dioxin and absolute lymphocyte count was found in both the unadjusted and adjusted analyses. In addition, a significant negative association between initial dioxin and the proportion of zero measurements was revealed in both the unadjusted and adjusted analyses of absolute basophils.

15.4.3 Model 3: Categorized Dioxin Analysis

Several contrasts that were marginally significant or significant in the unadjusted categorized dioxin analyses of the cell count variables and RBC morphology became nonsignificant or marginally significant in the adjusted analyses. A summary of the results of the categorized dioxin analysis is provided in Table 15-29. The contrast of Ranch Hands in the low dioxin category with Comparisons for RBC count was marginally significant without adjustment for covariates but nonsignificant after adjustment. When Ranch Hands in the high dioxin category were contrasted with Comparisons in the unadjusted, continuous analysis of WBC count, a significant difference was revealed. In the adjusted analysis the result was nonsignificant. The unadjusted contrast of Ranch Hands in the low dioxin category, with Comparisons in the discrete analysis of WBC count resulted in a significant difference, although the difference was marginally significant in the adjusted analysis. Continuous hemoglobin analysis revealed a marginally significant difference between Ranch Hands in the high category and Comparisons. In addition, analysis of RBC morphology revealed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons. After adjustment for covariates for both hemoglobin and RBC morphology, the results were nonsignificant. Except for the low Ranch Hand contrast for RBC count, each of the aforementioned contrasts displayed either a greater percentage of Ranch Hands with an abnormality or Ranch Hands with a higher cell count mean.

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	ns*	NS	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
White Blood Cell (WBC) Count (C)	ns	ns	+0.029	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	+0.027	ns	NS
Abnormal High vs. Normal	ns	ns	NS	NS
Hemoglobin (C)	ns	ns	NS*	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	NS	ns	ns	ns
Hematocrit (C)	ns	ns	NS	NS
Hematocrit (D)				
Abnormal Low vs. Normal	ns	ns	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
Platelet Count (C)	ns	ns	+<0.001	+0.017
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns*	ns*
Abnormal High vs. Normal	NS	ns	NS	ns
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	ns
RBC Morphology	NS	NS*	NS	NS
Absolute Neutrophils (Segs) (C)	ns	ns	+0.028	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS*	NS	+0.029
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	NS	ns	ns
Absolute Lymphocytes (C)	NS	ns	NS	ns
Absolute Monocytes (C)	ns	ns	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	NS	ns	NS
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	+0.025	NS	NS*

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Note: NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if p≤0.05.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Laboratory				
Red Blood Cell (RBC) Count (C)	NS	ns	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
White Blood Cell (WBC) Count (C)	NS	ns	NS	ns
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	NS	NS*	ns	NS
Abnormal High vs. Normal	ns	ns	NS	ns
Hemoglobin (C)	ns	ns	NS	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	NS	--	ns	--
Hematocrit (C)	ns	ns	NS	ns
Hematocrit (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	--	--	ns	--
Platelet Count (C)	ns	NS	+0.002	+0.038
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns*	ns*
Abnormal High vs. Normal	ns	--	NS	--
Prothrombin Time (C)	NS	ns	ns	ns
Prothrombin Time (D)	NS	NS	ns	ns
RBC Morphology	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS*	NS	+0.038
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Lymphocytes (C)	NS	ns	ns	ns
Absolute Monocytes (C)	ns	ns	NS	NS

Table 15-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	+0.009	NS	NS*

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥1.00 for discrete analysis; difference of means nonnegative for continuous analysis.
--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Results from the analyses of platelet count, both in the continuous and discrete forms, were consistent in the unadjusted and adjusted analyses. Significantly higher mean platelet counts were observed for Ranch Hands in the high and in the low and high dioxin categories combined than for Comparisons. The discrete analysis of platelet count revealed a marginally significant lower percentage of abnormally low platelet counts for Ranch Hands in the high and in the low and high dioxin categories combined than for Comparisons.

The analysis of the blood count variables revealed significant results for absolute neutrophils (segs) and absolute neutrophils (bands) in the continuous form and absolute basophils (zero versus nonzero measurements). A significant difference between Ranch Hands in the high dioxin category and Comparisons was found in the unadjusted analysis of absolute neutrophils (segs). The result was nonsignificant in the adjusted analysis. In both the unadjusted and adjusted analyses of absolute neutrophils (bands) in the continuous form, a marginally significant difference of means was found among Ranch Hands in the low dioxin category and Comparisons. Also, a significant absolute neutrophil (bands) mean difference was found among Ranch Hands in the low and high dioxin categories combined and Comparisons for both the unadjusted and adjusted analyses. Results were consistent in the unadjusted and adjusted analyses of absolute basophils (zero versus nonzero measurements). A significant difference in the proportion of zero absolute basophil measurements was found among Ranch Hands in the low dioxin category and Comparisons. A marginally significant difference was found when contrasting the low and high Ranch Hand dioxin categories with Comparisons. Both results indicate that more Ranch Hands than Comparisons had a zero absolute basophil measurement.

15.4.4 Model 4: 1987 Dioxin

In the unadjusted analyses, several significant and marginally significant results were found. The results are summarized in Table 15-30. Except for the analysis of the discrete form of WBC, each result became nonsignificant in the adjusted analysis. The significant association between continuous WBC count and 1987 dioxin was positive, as were the associations with continuous platelet count and absolute neutrophils (segs). Significant negative associations between 1987 dioxin and the percentage of abnormally low counts were revealed in the discrete analyses of WBC count, hemoglobin, and platelet count. In addition, a marginally significant negative association was found for the percentage of abnormally high hemoglobin counts and 1987 dioxin. For the blood count measures, a marginally significant positive association was found between absolute monocytes and 1987 dioxin.

Table 15-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
White Blood Cell (WBC) Count (C)	+0.013	NS
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	–0.020	–0.032
Abnormal High vs. Normal	ns	ns
Hemoglobin (C)	NS	NS
Hemoglobin (D)		
Abnormal Low vs. Normal	–0.049	ns
Abnormal High vs. Normal	ns*	ns
Hematocrit (C)	NS	NS
Hematocrit (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	+0.005	NS
Platelet Count (D)		
Abnormal Low vs. Normal	–0.028	ns
Abnormal High vs. Normal	ns	ns
Prothrombin Time (C)	ns	ns
Prothrombin Time (D)	ns	ns
RBC Morphology	NS	NS
Absolute Neutrophils (Segs) (C)	+0.017	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns
Absolute Lymphocytes (C)	NS	NS
Absolute Monocytes (C)	NS*	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	NS	ns

Table 15-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Absolute Basophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns

Note: NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative for continuous analysis.
–: Relative risk <1.00 for discrete analysis.

P-value given if $p\leq0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or differences of means nonnegative for continuous analysis. A lowercase "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

15.5 CONCLUSION

Five cell count measures, six measures of absolute blood counts, a coagulation measure, and RBC morphology were analyzed for the hematology assessment. In the analyses of these variables, only platelet count exhibited significant dose-response associations with the indices of dioxin exposure. Ranch Hands enlisted flyers and groundcrew exhibited slightly but significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than Comparisons in the continuous analysis. The results in the 1997 follow-up study parallel the findings of the 1987 and 1992 follow-up studies. In conclusion, apart from platelet count, there appears to be little evidence to support a relation between prior dioxin exposure and hematopoietic toxicity.

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